

LIPPINCOTT

# Q&A Medicine

Review for Clinical  
Rotations and Exams

**Editors:**

Mark D. Duncan

Lance W. Chapman

Minesh P. Shah

**Series Editors:**

Veeral S. Sheth

Stanley Zaslau

Robert Casanova



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## Review for Clinical Rotations and Exams

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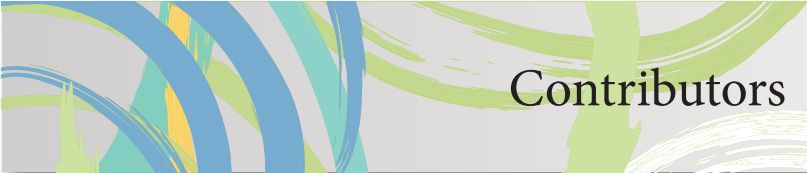
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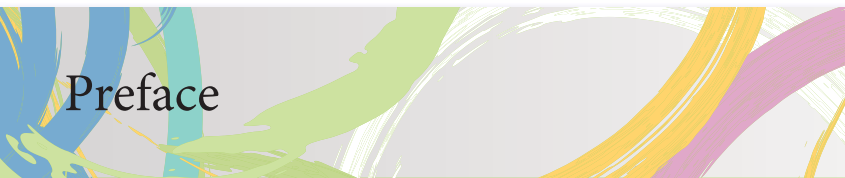
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# Preface

The Shelf-Life series was launched in 2014 with the Pediatrics, Surgery, and Obstetrics and Gynecology volumes leading the way. The books were designed from the ground up with student input at each phase of the process. The Lippincott Q&A Medicine volume builds on this foundation and takes the series a step further with a high-yield section we feel students will find extremely valuable. The Shelf-Life and Lippincott Q&A series are meant to help supplement the student's educational experience while on clinical rotation as well as prepare the student for the end-of-rotation shelf and subject examination. We are confident you will find these books challenging but an irreplaceable part of the clinical rotation. With high quality, up-to-date content, and hundreds of images and tables, these resources will be valuable beyond your rotation and well into your practice.

I would like to thank Susan Rhyner, for supporting this concept from its inception. I would like to express my appreciation to Tari Broderick, Amy Weintraub, Catherine Noonan, Laura Blyton, Amanda Ingold, Ashley Fischer, and Stacey Sebring, all of whom have been integral parts of the publishing team; their project management has been invaluable. Last, but not least, I would like to thank Monica, Sophia, and Sarina whose support before, during, and after this project is truly treasured.

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**Mark Duncan, MD**

I would like to thank Donovan Roy for providing the motivational support for the completion of this book. It was through his guidance and connection with students that several high-yield topics were included. Also, I want to thank my partner Tony for his enduring support throughout this exciting venture. Finally, this project would not have been possible without the mentorship and unparalleled guidance of Mark, Tari, Minesh, Veeral, and Amy. This book came to fruition as a result of a true team effort and I hope medical students find this tremendously useful for preparing for the internal medicine shelf examination!

**Lance Chapman, MD, MBA**



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# Cardiology

1

A 68-year-old man presents to the hospital with a 3-hour history of crushing substernal chest pain. He reports that the symptoms developed suddenly and were accompanied by sweating and nausea. The chest pain has been getting worse, is not exacerbated by deep inspiration, and does not radiate to his jaw or either arm. He endorses mild shortness of breath but denies subjective fevers, chills, headache, cough, abdominal pain, and diarrhea. He has a history of coronary artery disease, hypertension, diabetes, and gastroesophageal reflux disease (GERD). He takes aspirin, lisinopril, metformin, and omeprazole. His family history is significant for hypertension in both parents, and his father died of a heart attack at the age of 60. He has a 40 pack-year history of smoking, and denies any alcohol or illicit drug use. On examination, the patient is afebrile with a blood pressure of 150/96 mmHg, heart rate of 89 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation of 97% on room air. He appears diaphoretic. There is an S3 on cardiac auscultation, with mildly elevated jugular venous pulsations and bibasilar rales on pulmonary examination. His dorsalis pedis and posterior tibial pulses are diminished bilaterally, with mild swelling around his ankles. His initial laboratory values and ECG (Figure 1-1) are shown below.



Figure 1-1

|                     |                         |
|---------------------|-------------------------|
| Hemoglobin          | 14.2 g/dL               |
| Leukocyte count     | 9,000/mm <sup>3</sup>   |
| Platelets           | 275,000/mm <sup>3</sup> |
| Sodium              | 136 mEq/L               |
| Potassium           | 4.2 mEq/L               |
| Chloride            | 105 mEq/L               |
| Bicarbonate         | 22 mEq/L                |
| Blood urea nitrogen | 16 mg/dL                |
| Creatinine          | 1.2 mg/dL               |
| Glucose             | 145 mg/dL               |
| Calcium             | 9.6 mg/dL               |
| Troponin I          | Elevated                |

Which of the following best represents the underlying pathology in this patient?

- (A) Rupture of a plaque with thrombosis leading to partial occlusion of a coronary artery
- (B) Vasospasm of a coronary artery
- (C) Gradual occlusion of a coronary artery by plaque
- (D) Rupture of a plaque with thrombosis leading to complete occlusion of a coronary artery
- (E) Superficial erosion of a plaque with thrombosis

**The answer is D: Rupture of a plaque with thrombosis leading to complete occlusion of a coronary artery.** This is an extreme example of a long question that could be answered quickly if the reader first reads what the question is asking. This is a good strategy for long questions, since many students report that time management is challenging for the Medicine shelf examination. In this case, a brief survey of the question and answer choices would reveal that there is a process occurring that involves the patient's coronary arteries, and therefore all that is necessary is finding the diagnosis (obvious from the ECG) and then picking an answer choice. Much of the long history and examination is unnecessary, which can be skipped or at least skimmed; the laboratory tests are normal with the only significant finding being elevated troponins.



The ECG shows ST elevation in the inferior leads (II, III, aVF), confirming the diagnosis of ST elevation myocardial infarction (STEMI). The pathologic process occurring in a STEMI is most commonly due to rupture of an atherosclerotic plaque in the arterial wall of a coronary artery. Rupture of the plaque exposes tissue factor and other thrombogenic subendothelial components, leading to thrombosis and occlusion of the artery. (C) There is usually some degree of gradual narrowing of the artery due to the plaque, but rupture of the plaque with subsequent thrombosis is necessary to produce a STEMI. (A) The coronary artery occlusion is complete (not partial), which causes full thickness myocardial ischemia that manifests with ST elevations on ECG. (B) This answer refers to Prinzmetal angina, which is an unusual cause of myocardial ischemia that typically occurs in women with symptom onset in the evening. (E) Superficial erosion may occur but is not the most common mechanism in acute coronary syndromes (ACS).

2

A 62-year-old woman with a history of hypertension and hyperlipidemia presents to the hospital with diffuse muscle pain, weakness, and dark urine. She has no history of autoimmune or renal disease. Over the past month, she has had symptoms of cold intolerance, weight gain, and constipation. Her medications include hydrochlorothiazide, simvastatin, and gemfibrozil.

Urine dipstick reveals 3+ blood; however, there are no red blood cells on microscopic analysis. Some of the other laboratory values are shown below.

|                 |                |
|-----------------|----------------|
| Creatinine      | 2.3 mg/dL      |
| Creatine kinase | 34,000 U/L     |
| TSH             | 8.0 $\mu$ U/mL |

Which of the following is the most likely cause of her presentation?

- (A) Hashimoto thyroiditis
- (B) Pyelonephritis
- (C) Polymyositis
- (D) Medication effect

**The answer is D: Medication effect.** Muscle pain, weakness, and dark urine in the presence of an elevated creatine kinase (CK) should lead the reader to suspect rhabdomyolysis. This is further indicated by the blood on urine dipstick but no red blood cells on microscopy. Urine dipsticks bind hemoglobin and will be positive if there are red blood cells in the urine; however, myoglobin is similar in structure to hemoglobin and will also cause the dipstick to be positive in the absence of red blood cells on urine microscopy. CK is stored

within muscle and therefore is increased in the setting of significant muscle cell destruction. Statins are known to cause myopathies, ranging from benign myalgia to severe rhabdomyolysis. Hypothyroidism is a risk factor for developing severe myopathies while on a statin, and the patient's symptoms (weight gain, cold intolerance, and constipation) with an elevated TSH indicate that she has this risk factor. Another important risk factor for serious myopathies is the combination of a fibrate (e.g., gemfibrozil) and a statin. Initial treatment of rhabdomyolysis involves cessation of the offending agent (simvastatin) and correction of any fluid and electrolyte abnormalities.

(A) Hashimoto thyroiditis is the most common cause of hypothyroidism in developed countries, and may be the cause of this patient's hypothyroidism. However, this is the risk factor for the patient developing rhabdomyolysis and not the cause. (B) Pyelonephritis is inflammation of the kidney and the urinalysis will be consistent with a urinary tract infection. This would not cause an elevation in CK. (C) Polymyositis is an autoimmune condition that can be diagnosed by the presence of anti-Jo antibodies. There is some overlap with the symptoms (muscle pain and weakness with elevated CK), but polymyositis would not present so acutely (symptoms develop more subacutely to chronically).

3

A 47-year-old woman presents at night to the Emergency Department with chest pain. She states that the pain started that evening and has progressively been getting worse. She is concerned that she is having a heart attack. The pain is described as a burning sensation associated with a sour taste in her mouth, and it started shortly after she ate dinner; it has occurred on previous occasions, but never as bad as it is now. Previously, she used calcium carbonate tablets that were effective for the pain. She has no history of heart disease or other medical problems, and she takes no regular medications. She does not smoke cigarettes or use cocaine. Her vitals are normal, and her physical examination is unremarkable. Initial laboratory tests and an ECG are normal.

Which of the following is the most likely cause of this patient's chest pain?

- (A) Unstable angina
- (B) Myocarditis
- (C) Pulmonary embolism
- (D) Gastroesophageal reflux disease
- (E) Costochondritis

**The answer is D: Gastroesophageal reflux disease.** In a patient with a chief complaint of chest pain, it is important to consider life-threatening causes (e.g., myocardial infarction) as well as noncardiac causes of chest pain, which include disorders of the respiratory, GI, and musculoskeletal systems. This patient's history of recurrent burning chest pain after meals

that is associated with a sour taste in her mouth makes GERD the most likely diagnosis. Not all patients with ACS present with a classic history of retrosternal chest pain/pressure radiating to the jaw and left arm, so it is important to have a low index of suspicion for ACS in any patient (especially women and those with risk factors). Other cardiovascular causes of chest pain include any cause of angina (including Prinzmetal angina), pericarditis/myocarditis, and aortic dissection. Pulmonary causes include pneumonia, pulmonary embolism, pleuritis, and pneumothorax. Gastrointestinal causes include GERD, diffuse esophageal spasm, and peptic ulcer disease. Musculoskeletal causes include costochondritis, rib fracture, and muscle strain. Beyond these systems, psychiatric conditions (anxiety, panic disorder) and herpes zoster can both present as chest pain.

(A) Unstable angina is a type of ACS that presents without elevated cardiac enzymes and  $\pm$  ECG findings of ischemia. The history itself is not suggestive of a cardiac etiology. (B) Myocarditis is an inflammatory process of the heart muscle that is commonly the result of a viral process (e.g., Coxsackie). It presents as pleuritic chest pain with elevations in cardiac enzymes; it can lead to heart failure from poor ventricular function. (C) Pulmonary embolism will cause pleuritic chest pain, especially if it causes pulmonary infarcts. Look for this in a patient with risk factors (Virchow triad: blood stasis, endothelial injury, and a hypercoagulable state) and with tachycardia and tachypnea. (E) Costochondritis is caused by inflammation of the costal cartilage that connects the ribs to the sternum. The typical history is chest pain that is reproduced with palpation.

4

A 28-year-old woman frantically presents to the Emergency Department in the middle of the night with chest discomfort that awoke her from sleep. She has experienced similar episodes a few times before, always at night, but never as bad as this. She reports a history of migraines but denies any other medical history, including heart disease. Her medications include NSAIDs as needed and OCPs. She smokes a half pack of cigarettes a day but denies any alcohol or drug use. She admits that she gets “stressed out” a lot but believes that overall she lives a healthy lifestyle. Laboratory values show normal CK and troponin. An ECG shows ST elevations and she is taken for coronary angiography that does not show any significant coronary occlusions.

What is the most appropriate treatment for this patient?

- (A) Alprazolam
- (B) Diltiazem
- (C) Alteplase
- (D) NSAIDs
- (E) Reassurance

**The answer is B: Diltiazem.** High-dose calcium channel blockers are the preferred treatment for Prinzmetal angina. Sublingual nitroglycerin may also be prescribed to relieve chest pain during attacks and to minimize frequent visits to the Emergency Department. Smoking cessation is important and should be addressed.

This is a fairly classic presentation of Prinzmetal (variant) angina, which is caused by focal vasospasm of a coronary artery and typically occurs in young smokers that may have a history of other vasospastic disease (Raynaud, migraines, etc.). It usually occurs at night, and an ECG may show ST elevation as a result of transient myocardial ischemia that usually does not lead to infarction. During coronary angiography, vasospasm can be induced with the use of ergonovine, acetylcholine, or hyperventilation. Of note, this diagnosis can be differentiated from Takotsubo cardiomyopathy (can also present with ST elevations with normal coronary angiography) by the normal serum CK and troponin.

(A) Alprazolam is a benzodiazepine used for panic disorder. (C) Alteplase is a fibrinolytic used in acute myocardial infarction when PCI is unavailable. (D) NSAIDs may be used for viral pericarditis, but the sudden onset and recurrent description of the symptoms does not fit this diagnosis.

**5** A 73-year-old woman is brought in by paramedics after fainting in the mall and hitting her face. She does not remember any preceding symptoms, and she did not lose control of her bowel or bladder. Witnesses at the scene say that she was down for less than a minute, then woke up and was fairly alert. She was bleeding from a laceration on her chin and paramedics were called. When she arrived at the hospital, her initial laboratory values were normal and an EEG did not show epileptiform activity. She is placed on a cardiac monitor. The following day, she becomes lightheaded and loses consciousness while lying in bed, and her monitor shows tachycardia with the QRS complexes being uniformly longer than 120 ms.

What is the most common cause of this rhythm disturbance?

- (A) Uncontrolled hypertension
- (B) Distention of the pulmonary veins
- (C) Accessory pathway
- (D) Ischemic heart disease

**The answer is D: Ischemic heart disease.** The vignette describes an episode of ventricular tachycardia, which is indicated by the wide QRS complexes on her monitor. A serious arrhythmia should have been high on the differential given her episode of syncope with the red flag of head trauma, indicating a very sudden loss of consciousness without any ability to brace herself, which is typical of a cardiac etiology. The most common cause of ventricular tachycardia is ischemic heart disease. Patients that suffer a myocardial infarction have

scarring of the myocardium that disrupts the normal electrical pathways and increases the risk of developing this dangerous rhythm. (A, C) Uncontrolled hypertension and accessory pathways are not the most common causes of ventricular tachycardia. (B) Distention of the pulmonary veins is thought to be a mechanism of atrial fibrillation.

**6** A 63-year-old man presents to the Emergency Department after a fall, and he is found to have a broken hip. He undergoes surgical correction and recovers in the hospital. Before being discharged, he mentions to you that prior to the accident, he had not been able to exercise like before. For the past few months, he has experienced occasional chest pain with exertion that forces him to stop and rest. The pain goes away within 5 minutes of resting.

What should be performed before the patient is discharged from the hospital?

- (A) Pharmacologic stress test
- (B) Exercise stress test
- (C) Echocardiogram
- (D) Coronary angiography

**The answer is A: Pharmacologic stress test.** Although this is an unusual situation in that this history was not elicited before the patient underwent surgery, the point of the question is to assess the reader's knowledge on how to evaluate coronary artery disease. When a patient presents with symptoms of angina, it is important to make the diagnosis with a stress test. (B) An exercise stress test with ECG is the most common and preferred method for most patients; for patients that cannot undergo an exercise stress test like this patient with a broken hip, a pharmacologic stress test should be ordered. There are a variety of agents that may be used in this test (regadenoson, dobutamine, adenosine, dipyridamole), and the point is to stress the heart to the degree it would be stressed during exercise and assess for ischemic changes (ST depressions or elevations on ECG).

(C) An echocardiogram might be helpful to assess cardiac function and any valvular abnormalities, but it alone would not help in making the diagnosis of coronary artery disease unless it was done as part of a stress echo (looking for signs of ischemia that manifest as wall motion abnormalities). (D) Coronary angiography is an invasive procedure and may be performed after the stress test if the results are high risk or inconclusive.

**7** A 59-year-old woman presents to your office with chest discomfort, jaw pain, and nausea. The symptoms occurred suddenly 2 hours ago and are getting worse. She has a history of poorly controlled hypertension, and she has a 30 pack-year smoking history. You decide to send her

to the Emergency Department and order some initial tests, which are shown below.

|                     |           |
|---------------------|-----------|
| Sodium              | 137 mEq/L |
| Potassium           | 4.9 mEq/L |
| Chloride            | 105 mEq/L |
| Bicarbonate         | 22 mEq/L  |
| Blood urea nitrogen | 21 mg/dL  |
| Creatinine          | 1.3 mg/dL |
| Glucose             | 110 mg/dL |
| Troponin-I          | Positive  |

An ECG shows multiple T wave inversions and ST depressions in contiguous leads.

Which of the following is the most likely diagnosis?

- (A) Stable angina
- (B) Unstable angina
- (C) Non-ST elevation myocardial infarction
- (D) ST elevation myocardial infarction

**The answer is C: Non-ST elevation myocardial infarction.** It is important to know how to differentiate the types of ACS, since this guides the course of action as well as the prognosis. ACS is made up of unstable angina, non-ST elevation myocardial infarction (NSTEMI), and STEMI. (A, B) Stable angina is not an ACS, and typically occurs with a consistent level of exertion that is relieved with rest and/or nitroglycerin; however, it can progress to unstable angina which typically lasts less than 30 minutes and manifests as angina without exertion, angina with a crescendo pattern, or angina that is severe and of new onset. Any *new presentation* of typical angina is unstable angina, even if the description sounds like stable angina. (C, D) NSTEMI is differentiated from unstable angina by positive troponins, and STEMI is differentiated from NSTEMI by ST elevations seen on ECG. In unstable angina and NSTEMI, there may or may not be ST depression and T wave inversions (signs of myocardial ischemia), but there will not be ST elevations.



A patient suffers a myocardial infarction and undergoes percutaneous coronary intervention (PCI) with placement of a stent in the left anterior descending coronary artery. Later in the day, the patient develops

blue discoloration of several toes on both of his feet. The following day his creatinine increases from 1.2 to 1.8.

Which of the following best represents the mechanism in this situation?

- (A) Plaque disruption in the aorta
- (B) Plaque rupture and thrombosis in distal arteries of the legs
- (C) Emboli from vegetations present on a cardiac valve
- (D) Antibodies developed against myocardial antigens released during infarction
- (E) Consumption of platelets and small vessel hemorrhage in the extremities

**The answer is A: Plaque disruption in the aorta.** This is a case of cholesterol embolization syndrome, which is a rare complication of catheterization procedures (in this case, PCI). During PCI, a catheter is usually inserted into the femoral artery and advanced into the proximal aorta where the coronary arteries originate. During this process, disruption of atherosclerotic plaque in the aorta can cause embolization of cholesterol crystals distally. Patients with this syndrome present with multiple areas of ischemia, usually in small, distal vessels. They may also have renal injury and abdominal pain if vasculature to these areas are affected.

(B) Given the bilateral description of the findings, plaque rupture and thrombosis in the extremities is unlikely, since this would require that arteries in each extremity undergo the same process simultaneously. This process would also affect larger vascular territories than just the toes. (C) This choice refers to infective endocarditis, which is unlikely given the occurrence right after PCI was performed. (D) Dressler syndrome presents with pericarditis weeks after an MI. (E) Disseminated intravascular coagulation is unlikely given the focal findings in this patient.

9

A 33-year-old homeless man is brought into the Emergency Department by police after they found him barely arousable on the street next to an empty bottle of vodka. The patient has psychomotor slowing on examination, and a further history cannot be obtained. The ECG technician tells you that the patient has an abnormal heart rhythm.

Which of the following is the most likely diagnosis?

- (A) Sinus tachycardia
- (B) Second-degree heart block
- (C) Atrial fibrillation
- (D) Wolff-Parkinson-White
- (E) Polymorphic ventricular tachycardia

**The answer is C: Atrial fibrillation.** Atrial fibrillation is a common arrhythmia, and this patient is at risk from apparent alcoholism. Common causes of atrial fibrillation include hypertension and any underlying heart

disease, such as congestive heart failure (CHF), hypertrophic cardiomyopathy, previous myocardial infarction, and anything causing left atrial dilation. A useful mnemonic for remembering some of the causes of atrial fibrillation is *PIRATES*: Pulmonary disease, Ischemia, Rheumatic heart disease, Atherosclerosis/Atrial myxoma, Thyrotoxicosis, Ethanol, Sepsis. (A) Sinus tachycardia is an abnormal *rate* (not *rhythm*), so this does not answer the question. (B, D, E) Heart block, Wolff–Parkinson–White, and torsades de pointes are not nearly as common as atrial fibrillation in the general population or in alcoholics.



A 68-year-old man is brought in by ambulance after losing consciousness. The patient's wife was with him when he developed crushing chest pain while lying in bed. His wife went to get him some medication for the pain, but when she returned the patient was unconscious. Paramedics were called, and an ECG showed ST elevations in the anterolateral leads. His blood pressure is extremely low, and his extremities are cool.

Which of the following best represents the hemodynamics in this type of shock? (Note: CO is cardiac output, JVP is jugular venous pressure, SVR is systemic vascular resistance, and SvO<sub>2</sub> is mixed venous oxygen saturation.)

|     | CO | JVP | SVR | SvO <sub>2</sub> |
|-----|----|-----|-----|------------------|
| (A) | ↑  | ↓   | ↓   | ↑                |
| (B) | ↓  | ↑   | ↑   | ↓                |
| (C) | ↓  | ↓   | ↑   | ↓                |
| (D) | ↓  | ↓   | ↓   | ↓                |

**The answer is B: Decreased CO, increased JVP, increased SVR, decreased SvO<sub>2</sub>.** Cardiogenic shock can result from any process leading to ventricular failure, such as myocardial infarction, arrhythmias, acute valvular changes (e.g., acute mitral regurgitation), myocarditis, cardiac contusion, and exacerbated CHF. A decrease in cardiac output will manifest with distended neck veins and cool extremities since peripheral vessels will constrict (increased SVR) to preserve blood pressure. SvO<sub>2</sub> indicates the oxygen saturation of hemoglobin in blood returning to the right side of the heart. In most causes of shock the SvO<sub>2</sub> will be low due to poor circulatory function and increased tissue extraction of oxygen. SvO<sub>2</sub> can be elevated in some forms of distributive shock (e.g., sepsis) due to a high flow state in which there is insufficient time for the peripheral tissues to extract oxygen from the circulating red blood cells. This patient suffered a myocardial infarction that led to cardiogenic shock.

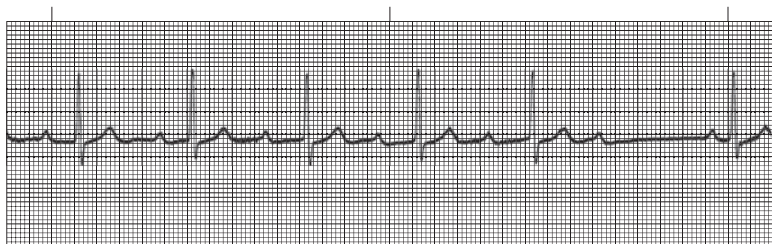


Obstructive shock is a category in which the primary problem is not failure of the heart, but is an obstruction in the circulatory system that disrupts blood flow. Examples include pulmonary embolism, tension pneumothorax, and cardiac tamponade. This will present with the same hemodynamics given in the answer choice for cardiogenic shock; however, the two categories can be differentiated based on the history, physical examination, and other targeted studies.

(A) Examples of distributive shock include sepsis, anaphylaxis, adrenal insufficiency, and spinal cord injury (neurogenic shock). The primary problem in this form of shock is an inability to maintain SVR. The CO may be high initially but then will decrease over time due to cardiac fatigue. (C) In hypovolemic shock, SVR is increased as a response to maintain blood pressure but the CO is normal or low due to the decrease in preload. (D) This scenario could be seen in distributive forms of shock when the heart begins to fail, leading to a decrease in CO and subsequently SvO<sub>2</sub> due to slowing of the previously high flow state.

**11** While rounding with the team, a nurse asks you to come see a patient recovering from pneumonia who has developed an unusual rhythm on his monitor (*Figure 1-2*).

The patient reports that he does not feel weak or have any palpitations, and his vitals are normal. His medical history is only significant for hypertension, for which he takes diltiazem. He has no family history of heart disease and does not smoke. You attempt a carotid sinus massage, and you see that there are more dropped beats on the monitor.



**Figure 1-2**

Which of the following is the most appropriate next step in management?

- (A) Decrease his dose of diltiazem
- (B) Increase his dose of diltiazem
- (C) Cardioversion
- (D) Administer amiodarone
- (E) Administer atropine
- (F) Start heparin and warfarin, and stop the heparin once his INR is therapeutic

**The answer is A: Decrease his dose of diltiazem.** The rhythm shown in the ECG is second-degree atrioventricular (AV) block, Mobitz type I (also known as Wenckebach). This is a benign rhythm disturbance caused by abnormal conduction through the AV node that causes a gradual prolongation of the PR interval with each beat until a beat is dropped. Vagal stimulation (e.g., carotid sinus massage) can increase the parasympathetic tone in the AV node and worsen the condition, causing more dropped beats. This is in contrast to Mobitz II, another type of second-degree AV block that shows a fixed PR interval with occasional dropped beats that improves with vagal stimulation.

First-degree AV block presents with a prolonged PR interval ( $>200$  ms) without any dropped beats. Third-degree AV block presents with complete AV dissociation, in which there is no conduction through the AV node. Pacemaking cells beyond the AV node, which have a slower inherent rate and are normally suppressed by proximal pacemaking cells (override suppression), now fire independently from the atrial impulse as an escape rhythm. First-degree and second-degree Mobitz I are relatively harmless and generally do not require treatment. Mobitz II can progress to third-degree AV block, and therefore both of these conditions require a pacemaker.

(B) Increasing the dose of his calcium channel blocker would slow conduction through the AV node further and exacerbate the condition. (E) Giving atropine would improve AV conduction, but no treatment is required in this case. (C, D, F) This is a harmless rhythm that does not require cardioversion, anti-arrhythmics, or anticoagulation.



**12** A 53-year-old man is hospitalized with pneumonia and is placed on a cardiac monitor. While in the room, you notice that he is in normal sinus rhythm but has occasional wide complexes without any pattern or relationship to the cardiac cycle. They occur several times per minute. The patient states that every once in awhile he feels like his heart skips a beat. He has no history of heart disease or sudden death in the family, and his vitals are normal.

Which of the following is the most appropriate next step in management?

- (A) Catheter ablation of the ectopic focus
- (B) Administer metoprolol
- (C) Administer propafenone
- (D) Avoidance of caffeine and other stimulants

**The answer is D: Avoidance of caffeine and other stimulants.** Premature ventricular contractions (PVCs), also known as ventricular premature beats, are very common electrical disturbances that are usually benign. They are concerning if they occur frequently, are symptomatic,

or occur in a patient with structural heart disease (e.g., previous myocardial infarction). The presence of occasional PVCs in a structurally normal heart may be associated with an increased mortality; however, the use of prophylactic medications or procedures has not been shown to affect mortality. For the shelf examination, the right answer for a “next step in management” question is often the least invasive option (e.g., lifestyle modification), and therefore the patient should avoid any triggers of PVCs. (A, B, C) Occurrence of PVCs is extremely common (occur in about 80% of healthy patients); catheter ablation,  $\beta$ -blockers, and anti-arrhythmics are not likely to be helpful or cost effective. These options may be pursued in the setting of frequent or symptomatic PVCs if trigger avoidance fails to resolve the symptoms.

13

A 48-year-old man presents to the hospital after passing out during a basketball game with his friends. He was running toward the basket when he “blacked out.” He does not remember how long he was out, but he does remember waking up. On examination, his vitals are normal. Cardiac examination reveals a 3/6 midsystolic crescendo-decrescendo murmur heard best over the right upper sternal border, which radiates to the carotid arteries. The rest of the examination, including a neurologic examination, is normal. An ECG suggests left ventricular hypertrophy.

Which of the following symptoms carries the worst prognosis in this condition?

- (A) Dyspnea from pulmonary edema
- (B) Angina
- (C) Syncope
- (D) Palpitations

**The answer is A: Dyspnea from pulmonary edema.** This patient presents after an episode of syncope, with the murmur of aortic stenosis on examination. Because he is relatively young, he likely has aortic stenosis as a result of a congenital bicuspid valve. Once patients develop symptoms, they require surgical aortic valve replacement or else the prognosis is poor. (B, C) The typical symptoms of aortic stenosis can be remembered using the mnemonic ASD, which also relates to the mean survival once symptoms develop: Angina (mean survival 5 years), Syncope (mean survival 3 years), and Dyspnea from heart failure (mean survival 2 years). This patient experienced syncope as a result of decreased cerebral perfusion, which occurs due to an inability of the heart to increase cardiac output (fixed obstruction) in the setting of peripheral vasodilation during exercise. (D) Though patients with aortic stenosis often develop atrial fibrillation, the development of palpitations would not necessarily qualify a patient as having “symptomatic aortic stenosis” and does not correlate with mortality.

**14** A 56-year-old man was recently hospitalized for an acute myocardial infarction. He was treated appropriately and had no complications during his hospitalization. After discharge, he follows up regularly in your clinic. Several months after his hospitalization, he comes to clinic for a regular visit with no complaints, stating that he is tolerating his new medications well. As he begins to leave, he mentions problems during intercourse with his wife and asks if he could have a prescription for sildenafil. A further history is obtained, and he reports that he no longer has morning erections.

Which of the following is most likely responsible for this complaint?

- (A) Lisinopril
- (B) Metoprolol
- (C) Amlodipine
- (D) Atorvastatin
- (E) Psychosocial stressors

**The answer is B: Metoprolol.**  $\beta$ -blockers have a high incidence of erectile dysfunction as a side effect. Since he just recently suffered a myocardial infarction, it is assumed that he is now taking the standard discharge medications (dual antiplatelet therapy,  $\beta$ -blocker, ACE inhibitor, statin). (A) ACE inhibitors may cause cough and hyperkalemia, and they are teratogenic. They should be avoided in patients with hereditary angioedema (C1 esterase inhibitor deficiency) since there will be rapid accumulation of bradykinin causing angioedema. (C)  $\beta$ -blockers are preferred to calcium channel blockers after myocardial infarction. (D) Statins may cause myopathies and elevation of transaminases, but not erectile dysfunction. (E) Psychosocial stressors are a common cause of erectile dysfunction; however, this patient just started a medication that commonly causes erectile dysfunction and so this is the more likely answer. In addition, the lack of morning erections indicates an organic etiology rather than psychosocial problems.

**15** A 72-year-old man presents to the Emergency Department complaining of chest pain. The patient is afebrile with a blood pressure of 104/68 mmHg, heart rate of 112 beats per minute, respiratory rate 14 breaths per minute, and oxygen saturation of 97% on room air. The patient has jugular venous distention and his lungs are clear to auscultation bilaterally. An ECG shows ST elevation in leads V1 and V2, and a right-sided ECG shows ST elevation in V4R.

Which therapy should NOT be given at this time?

- (A) Intravenous normal saline
- (B) Aspirin
- (C) Nitroglycerin
- (D) Lisinopril
- (E) Atorvastatin

**The answer is C: Nitroglycerin.** Nitroglycerin is a nitrate medication that is used to relieve anginal pain. It works by causing the release of nitric oxide in smooth muscle, which increases intracellular cGMP leading to vascular relaxation. Its effect is more pronounced on veins than arteries, especially at low doses, so the major effect will be venodilation that reduces preload to the heart and thus decreases myocardial oxygen demand. This is thought to be the mechanism of relieving anginal pain, and not coronary artery dilatation (since the coronary arteries are maximally dilated in response to ischemia during angina).

In the situation described above, nitroglycerin is not recommended for two reasons: first, it may lead to hypotension (by causing peripheral vasodilation), and second, it is dangerous in a patient with a right ventricular infarct. Although rare, a right ventricular infarct can cause poor functioning of the right ventricle with a relatively normal left ventricle that can sustain cardiac output as long as there is sufficient preload coming from the right ventricle. It is important to maintain adequate filling pressures (preload) to the right ventricle to ensure that enough blood is getting to the left ventricle. Right ventricular infarcts are therefore preload dependent, and intravenous (IV) normal saline can be provided if the patient is hypotensive. Nitroglycerin would decrease preload through its action as a venodilator, reducing cardiac output and exacerbating the patient's hypotension. Likewise, morphine should be avoided since it also causes venodilation and decreases preload.

The right ventricular infarct is suggested by the patient's jugular venous distention with clear lung fields, implying that the "obstruction" is proximal to the lungs. On ECG, ST elevation in leads V1–V2 can be seen in a right ventricular infarct; however, ST elevation in V4R (right-sided chest leads) is the most sensitive finding. (A, B, D, E) The other answer choices are appropriate in patients presenting with ACS, although IV fluids are not usually given in the setting of left ventricular dysfunction since the excess preload can worsen cardiac output. Although lisinopril is an ACE inhibitor and acts as a diuretic, it is usually safe to give in patients with a systolic blood pressure over 100 mmHg.

16

A 48-year-old man presents to the hospital with swelling of the abdomen and legs. He first noticed shortness of breath with exertion several months ago, and has had a few episodes where he momentarily became lightheaded and lost consciousness. Now the symptoms have been progressing with increased dyspnea and edema. He reports that he has always lived a healthy lifestyle and has no past medical history. There is no family history of any cardiac or pulmonary disease, or any cancer. He was born in Brazil and moved to the United States at the age of 43. He does not smoke or drink alcohol. On cardiac examination, the apex is displaced laterally with an S3 on auscultation. Estimated central

venous pressure is 15 mmHg, and there are faint crackles at the base of his lungs. He has hepatomegaly with shifting dullness and bilateral pitting edema of the lower extremities. An ECG is normal, with no visible Q waves.

Which infectious etiology is most likely responsible for this patient's disease?

- (A) *Mycobacterium tuberculosis*
- (B) *Staphylococcus aureus*
- (C) *Streptococcus pneumoniae*
- (D) *Borrelia burgdorferi*
- (E) Coxsackie B virus
- (F) Influenza virus
- (G) Human immunodeficiency virus
- (H) *Paracoccidioides brasiliensis*
- (I) *Coccidioides immitis*
- (J) *Trypanosoma cruzi*
- (K) *Echinococcus granulosus*
- (L) *Entamoeba histolytica*

**The answer is J: *Trypanosoma cruzi*.** The most common cause of non-ischemic cardiomyopathy in Latin America is Chagas disease. This patient has evidence of dilated cardiomyopathy and is in heart failure based on the symptoms and physical examination. In addition, he has had several episodes of syncope that are likely the result of arrhythmias. *Trypanosoma cruzi* is a parasite transmitted in the feces of the reduviid bug. The initial infection is commonly asymptomatic, but if untreated it can result in chronic Chagas heart disease, which may include chest pain, arrhythmias, heart failure, and thromboembolic disease. Once the disease has reached the chronic phase, it is irreversible. Treatment of the acute infection is with either benznidazole or nifurtimox, but treatment for chronic Chagas heart disease is the same as for other causes of heart failure. In a younger patient from Latin America with no atherosclerotic risk factors who presents with heart failure, consider Chagas heart disease as a potential diagnosis.



**17** A 62-year-old man presents to the hospital with chest pain and shortness of breath. The symptoms started suddenly 2 hours ago, when he experienced a squeezing sensation in his chest and began to get short of breath. He has a history of hypertension and diabetes. On examination, the patient has a blood pressure of 104/63 mmHg with a heart rate of 105 beats per minute and a respiratory rate of 22 breaths per minute. He appears diaphoretic with a 2/6 blowing systolic murmur at the apex that radiates to his axilla. Rales are heard bilaterally over the lung bases. An ECG is performed and is shown in Figure 1-3.

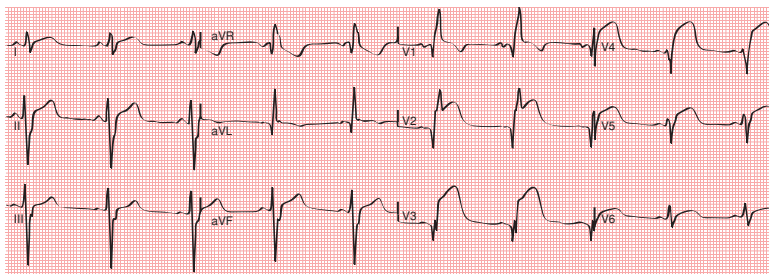


Figure 1-3

The hospital is not equipped to perform PCI, and the nearest hospital with a catheterization laboratory is 15 minutes away. Which of the following is the best next step in management?

- (A) Transfer the patient for PCI
- (B) Start ibuprofen and colchicine
- (C) Start fibrinolytics
- (D) Arrange for emergency valvular surgery

**The answer is A: Transfer the patient for PCI.** This patient is presenting with STEMI and requires urgent reperfusion of his coronary arteries. The earlier the intervention, the more amount of myocardium that is saved. There are two options for reperfusion: mechanical reperfusion with PCI and stent placement, or chemical reperfusion with fibrinolytics. For most patients, PCI is the treatment of choice; however, not all hospitals have a catheterization laboratory with dedicated cardiologists on call all the time. If PCI is to be most effective, the door-to-balloon time (the time from which the patient presents to the time they undergo catheterization) should be less than 90 minutes, although up to 120 minutes is still acceptable. If this time limit cannot be achieved, the fibrinolytics should be given within 30 minutes after contraindications are assessed (such as previous intracerebral hemorrhage, intracranial tumor/aneurysm, active internal bleeding). (C) This patient should be transferred to the hospital 15 minutes away for PCI rather than fibrinolytics.

(D) The patient has a murmur of mitral regurgitation, which can be seen in acute myocardial infarctions; however, emergency valvular surgery is not treating the underlying problem of coronary artery occlusion. (B) Ibuprofen and colchicine would be appropriate therapies for acute pericarditis; however, the patient does not have a suggestive history and the ECG does not show diffuse ST elevations in all leads.

18

A 49-year-old African American woman presents with sharp chest pain and difficulty breathing. For the past few months, she has had similar symptoms but could manage by decreasing her activity. Over

the past few days, her symptoms have worsened and she experiences severe chest pain with each inspiration; she has been bedridden over this time. A review of systems is significant for an unintentional weight loss of 6.8 kg (15 lb) over the past few months. She has no past medical history and has not been to a doctor since she was a child. She takes no medications. The patient’s vitals show a blood pressure of 138/88 mmHg with a heart rate of 112 beats per minute and respiratory rate of 28 breaths per minute. Cardiovascular examination reveals distended neck veins, and her lungs are clear to auscultation bilaterally. There is hepatomegaly with lower-extremity edema. She is admitted, and a CT with contrast shows a large thrombus in the inferior vena cava with thrombi in multiple small pulmonary vessels. She is eventually diagnosed with ovarian cancer and receives anticoagulation, with subsequent CT imaging showing pulmonary vasculature without any thromboemboli; however, she continues to have distended neck veins and episodes of hypotension.

A pulmonary artery catheter is advanced through the internal jugular vein to record pressures within the heart. Which of the following recordings most accurately reflect the pressures found by Pulmonary artery in this patient? (Note: SVC is superior vena cava, RA is right atrium, RV is right ventricle, PA is pulmonary artery, and PCWP is pulmonary capillary wedge pressure.)

|     | SVC       | RA        | RV        | PA        | PCWP      |
|-----|-----------|-----------|-----------|-----------|-----------|
| (A) | Normal    | Normal    | Normal    | Normal    | Normal    |
| (B) | Normal    | Normal    | Normal    | Increased | Increased |
| (C) | Increased | Increased | Increased | Normal    | Normal    |
| (D) | Increased | Increased | Increased | Increased | Normal    |
| (E) | Decreased | Decreased | Decreased | Decreased | Decreased |

**The answer is D: Increased SVC, increased RA, increased RV, increased PA, normal PCWP.** This patient is suffering from pulmonary hypertension from chronic thromboembolic events (WHO classification group 4). Although she is presenting with acute decompensation likely from an increase in clot burden, her symptoms started several months ago, suggesting a chronic process. Her underlying ovarian cancer is causing a hypercoagulable state, and she has been bedridden for the past few days, both of which contribute to further clot formation. Chronic thromboemboli to the lungs cause obstruction in blood flow, which increases the pressure in the right side of the heart. Over time, pulmonary hypertension will lead to right heart failure, which is manifested



by distended neck veins, hepatomegaly, and peripheral edema. Pulmonary artery catheterization is a method for measuring pressures within the right side of the heart. In addition, it can accurately estimate left atrial pressure by the PCWP, which should be normal given that the left atrium is distal to the disease process.

**19** A 57-year-old woman with hypertension and end-stage renal disease presents to the hospital with worsening confusion and hypotension. According to her husband, she has been compliant with her medications and diet. She receives dialysis 2 times weekly, with her last session occurring 2 days ago. On examination, she is hypotensive with distant heart sounds and distended neck veins. An echocardiogram is performed which shows a moderate amount of pericardial fluid with collapse of the right atrium during diastole. A blood pressure cuff is placed on the patient and she is asked to take a deep breath.

Which of the following changes will take place during inspiration? (Note: RV is right ventricle, LV is left ventricle, PVC is pulmonary vascular compliance.)

|     | Blood Pressure | RV Volume | LV Volume | PVC       |
|-----|----------------|-----------|-----------|-----------|
| (A) | Decreased      | Increased | Decreased | Increased |
| (B) | Decreased      | Decreased | Decreased | Decreased |
| (C) | Decreased      | Decreased | Decreased | Increased |
| (D) | Increased      | Increased | Decreased | Decreased |

**The answer is A: Decreased blood pressure, increased RV volume, decreased LV volume, increased PVC.** This patient is presenting with Beck’s triad of cardiac tamponade: distant heart sounds, elevated jugular venous pressure, and hypotension. Patients with a history of advanced renal disease are at risk for uremic pericarditis, which may or may not present with chest pain. Effusions are typically present and may develop into tamponade. In cardiac tamponade, the surrounding pericardial fluid causes equalization of pressure within the four heart chambers and leads to obstruction of blood flow without pulmonary edema. During inspiration, the negative intrathoracic pressure draws blood into the right ventricle, increasing the volume of the right ventricle and causing the interventricular septum to shift and decrease the volume of the left ventricle. In addition, pulmonary vascular compliance is increased during inspiration (increased volume of the lung parenchyma and vasculature), which also decreases

preload to the left ventricle. This results in a reduced stroke volume of the left ventricle and a decrease in blood pressure. Although a small decrease in systolic blood pressure occurs in healthy patients during inspiration, a decrease  $\geq 10$  mmHg is defined as pulsus paradoxus and is commonly seen with cardiac tamponade.

Treatment of uremic pericarditis involves increasing the frequency or duration of hemodialysis. Because she is currently having tamponade physiology, she will require pericardiocentesis to remove the pericardial fluid.



A 65-year-old woman presents to the hospital complaining of difficulty breathing. She reports that the symptoms have developed over the past few weeks, starting with leg swelling. She was previously eating well and exercising several times weekly, but admits that the past month has been extremely busy so her diet and exercise has suffered. She now cannot walk to her mailbox without becoming short of breath. She has a history of hypertension but admits that she does not regularly take her medication. Her blood pressure is currently 158/104 mmHg. She has an S4 on cardiac examination, with an elevated estimated central venous pressure. On examination of her lungs, she has dullness to percussion at the bases with wet rales halfway up the lung fields. She has pitting edema around her ankles. An echocardiogram shows a normal ejection fraction.

Based on this patient's likely diagnosis, which of the following treatments have been shown to reduce mortality?

- (A) ACE inhibitor
- (B) Angiotensin receptor blocker
- (C) Aldosterone antagonist
- (D)  $\beta$ -blocker
- (E) All of the above
- (F) None of the above

**The answer is F: None of the above.** This patient is presenting in CHF with evidence of diastolic dysfunction. Heart failure can generally be divided into two categories: systolic dysfunction (reduced ejection fraction) and diastolic dysfunction (preserved ejection function). Causes of diastolic dysfunction include hypertension, ischemia, hypertrophic and restrictive types of cardiomyopathies, and aortic stenosis. In hypertension, the increased afterload experienced by the left ventricle leads to increased pressure work, and the heart responds by remodeling with concentric hypertrophy. The myocardial wall thickens and becomes stiff, losing its ability to relax (loss of compliance) and allow a sufficient volume of blood to be pumped out during systole (although the *proportion* of blood volume ejected during systole

remains the same). This patient has a history of hypertension with findings of CHF on examination, as well as an S4 which make the likely diagnostic category diastolic dysfunction.

Heart failure with systolic dysfunction often leads to a dilated cardiomyopathy with eccentric hypertrophy (dilation) as a response to increased volume work. This type of heart failure will present with findings of CHF on examination and an S3. Many trials have shown that certain medications reduce the mortality in patients with systolic dysfunction: ACE inhibitors, angiotensin receptor blockers,  $\beta$ -blockers, aldosterone antagonists, omega-3 fatty acids, cardiac resynchronization therapy, implantable cardiac defibrillator, and hydralazine with nitrates (especially in African Americans). Unfortunately, these medications have not been shown to reduce mortality in patients with diastolic dysfunction.

**21** A 68-year-old woman is admitted for shortness of breath and is found to be in heart failure. Her blood pressure is 140/60 mmHg, with a heart rate of 102 beats per minute. When you examine her, you notice that her carotid arteries have a noticeably brisk rise and fall. When you apply pressure to her fingernails, you see subungual pulsations.

Which of the following findings on cardiac examination is most likely?

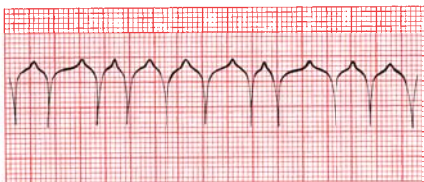
- (A) Midsystolic crescendo–decrescendo murmur at the right upper sternal border
- (B) Diastolic decrescendo murmur at the left upper sternal border
- (C) Holosystolic blowing murmur at the apex
- (D) Early diastolic opening snap followed by a low-pitched rumble

**The answer is B: Diastolic decrescendo murmur at the left upper sternal border.** This represents the murmur of aortic regurgitation (aortic insufficiency), which is the cause of this patient's acute heart failure. Hints to the diagnosis come from the widened pulse pressure ( $>40$  mmHg), the brisk rise and fall of her pulse ("water hammer" pulse, A.K.A. Corrigan pulse), and the subungual pulsations (Quincke sign). Though these are not all sensitive and specific signs, together they make the likely diagnosis of aortic regurgitation.

(A) This is the murmur of aortic stenosis, which radiates to the carotid arteries. Other examination findings would be *parvus et tardus* (delayed carotid upstroke), and a left ventricular heave with an S4 in advanced disease. (C) Mitral regurgitation presents with this murmur, which radiates to the axilla. There can also be a split S2 (aortic valve closing early) and atrial fibrillation from left atrial enlargement. An S3 might be heard in advanced disease. (D) Mitral stenosis presents as a diastolic murmur with an opening

snap. Like mitral regurgitation, it can cause left atrial enlargement and atrial fibrillation.

- 22** A 68-year-old woman with chronic obstructive pulmonary disease (COPD) comes to the hospital because of 3 days of fatigue and worsening dyspnea. She has no history of hypertension or heart disease. Her blood pressure is 102/58 mmHg with a heart rate of 142 beats per minute. The jugular venous waveform is monophasic. An ECG is taken and shown below (*Figure 1-4*).



**Figure 1-4**

Which of the following is the first step in management of this condition?

- (A) Start aspirin
- (B) Start heparin and warfarin
- (C) Immediate cardioversion
- (D) Start diltiazem
- (E) Start amiodarone
- (F) Start propranolol

**The answer is D: Start diltiazem.** The ECG above shows an irregularly irregular rhythm with no distinct P waves, confirming the diagnosis of atrial fibrillation. It also shows a fast rate, which is called atrial fibrillation with rapid ventricular response. The venous waveform will be monophasic due to loss of the atrial kick (a wave), leaving only the v wave. Many patients are asymptomatic from atrial fibrillation, since two-thirds of left ventricular filling occurs during diastole with the atrial kick only contributing one-third of the preload to the left ventricle. Older patients or those with underlying cardiac disease will often be symptomatic.

(C) This is the patient's first known episode of atrial fibrillation; she is currently stable and therefore does not require immediate cardioversion. The first step in stable patients is rate control with a  $\beta$ -blocker or calcium channel blocker (another option is digoxin). (F) A calcium channel blocker such as diltiazem is preferred over a  $\beta$ -blocker given the patient's COPD; propranolol is a nonselective  $\beta$ -blocker and therefore would cause bron-

chospasm due to blockade of  $\beta_2$  receptors. (E) Amiodarone is another option for rate control, but would be a bad idea in this patient since it can cause chemical cardioversion and cause embolization of a thrombus if one is present.

After rate control is achieved (goal resting heart rate  $<110$  beats per minute according to the RACE II trial), the patient should be anticoagulated since there is a risk of thrombus formation in the left atrium (usually in the atrial appendage) that can embolize to the brain and cause a stroke. Patients with new onset atrial fibrillation less than 48 hours can undergo cardioversion (low risk of stroke), but in patients with onset greater than 48 hours ago (this patient) there are two options: either the patient can have a transesophageal echocardiogram to rule out a left atrial thrombus before cardioversion, or they can start empiric anticoagulation for at least 3 weeks before cardioversion is attempted. After cardioversion is completed, all patients must have at least 4 weeks of anticoagulation unless there are serious contraindications.

(A) Aspirin should be given in chronic atrial fibrillation when the CHADS<sub>2</sub> score is 0 or 1. (B) Anticoagulation will be given to this patient, but it is not the first step in management. (Note: the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is a newer model for estimating the risk of stroke in patients with atrial fibrillation; however, the CHADS<sub>2</sub> score is sufficient for the shelf examination.)

23

A 52-year-old woman presents to the hospital with a severe headache and nausea. She has no history of headaches and is concerned that she is having a stroke. Her medical history is significant for long-standing hypertension, diabetes, and GERD. She admits that she is not always compliant with her medications, and recently ran out of them. Her blood pressure is 193/124 mmHg, and fundoscopic examination reveals papilledema. The rest of her physical examination, including a neurologic examination, is normal.

Which of the following is the correct diagnosis and treatment?

- (A) Hypertensive urgency; gradual lowering of blood pressure with oral agents
- (B) Hypertensive urgency; rapid lowering of blood pressure with IV agents
- (C) Hypertensive emergency; gradual lowering of blood pressure with oral agents
- (D) Hypertensive emergency; rapid lowering of blood pressure with IV agents

**The answer is D: Hypertensive emergency; rapid lowering of blood pressure with IV agents.** Hypertensive urgency is defined as a systolic blood pressure  $>180$  mmHg and/or a diastolic blood pressure  $>120$  mmHg

with no end-organ damage. Hypertensive emergency is the same definition with the addition of end-organ damage. Many organs are acutely affected by high blood pressure, including the brain (stroke), eyes (papilledema), heart (aortic dissection), lungs (pulmonary edema), and kidneys (renal failure). Within the umbrella term of hypertensive emergency, there are additional terms for specific end-organ involvement: malignant hypertension refers to hypertensive emergency in the presence of papilledema (other ophthalmologic findings include retinal exudates and hemorrhage), and malignant nephrosclerosis refers to renal damage. This patient has a hypertensive emergency with end-organ involvement including the brain (headache) and the eyes (papilledema).

**(A, B, D)** The management of hypertensive urgencies and emergencies is slightly different. In hypertensive urgency, the goal is to gradually lower the blood pressure to achieve a normal value within a couple of days. Oral antihypertensive agents are given while monitoring the reduction in blood pressure over hours. Some options for oral medications include labetalol, captopril, clonidine, furosemide, and hydralazine. In hypertensive emergency, there is ongoing end-organ damage and therefore blood pressure needs to be lowered quickly. The goal in this setting is to immediately lower blood pressure using IV agents, targeting a decrease in mean arterial pressure by 25% within minutes to hours. Some options for IV medications include nitroprusside, nitroglycerin, calcium channel blockers (e.g., nicardipine), labetalol, hydralazine, fenoldopam, and phentolamine. Because adaptive mechanisms occur with chronically elevated blood pressure, rapid lowering of blood pressure is not always tolerated and can cause cerebral hypoperfusion. If this happens, the blood pressure must be lowered more gradually.

**24**

A 68-year-old woman presents with progressive dyspnea. She has a history of longstanding hypertension, previous myocardial infarction, and several episodes of ventricular tachycardia that required cardioversion. She is now maintained on prophylactic medication with good cardiac function and no further arrhythmias. On examination, she is afebrile with a respiratory rate of 28 breaths per minute and oxygen saturation of 92% on room air. Cardiac examination is normal, but she has dry rales throughout her lung fields. A CT scan of the chest shows diffuse ground-glass opacities.

Which medication is most likely responsible for the patient's symptoms?

- (A)** Digoxin
- (B)** Lisinopril
- (C)** Amiodarone
- (D)** Bleomycin

**The answer is C: Amiodarone.** Amiodarone is an anti-arrhythmic medication that may be used for prophylaxis or treatment of serious arrhythmias, especially ventricular arrhythmias. This patient has a history of ventricular tachycardia, and therefore has an indication to be taking amiodarone. This drug has much toxicity, and therefore when started the patient must have baseline pulmonary function tests, thyroid function tests, and liver function tests due to the toxicity involving each of these organs. Other notable side effects include blue-gray discoloration of the skin, corneal deposits, and peripheral neuropathy. This patient developed pulmonary fibrosis as a result of chronic amiodarone use. (A, B) Digoxin and lisinopril are not associated with pulmonary fibrosis. (D) Bleomycin can cause pulmonary fibrosis, but it is an antineoplastic drug and the patient has no reason to be taking this medication.

25

A 41-year-old woman presents to the hospital with shortness of breath that developed over the last 2 weeks. She has also noticed progressive swelling in her legs. She sleeps with four pillows at night and sometimes wakes up in the middle of the night gasping for air. On review of systems, she mentions that over the past year she has been increasingly anxious with frequent perspiration and diarrhea. She has no significant medical history and takes no medications. The patient is afebrile with a blood pressure of 143/88 mmHg, heart rate of 107 beats per minute, and respirations of 30 breaths per minute with an oxygen saturation of 93% on room air. She appears anxious and is mildly diaphoretic. Her cardiac examination shows a regular rhythm, a 2/6 systolic murmur heard at best at the left upper sternal border, and an estimated central venous pressure of 14 mmHg. In addition, she has wet rales heard along the lung bases and 2+ pitting edema bilaterally to the level of her knees. Laboratory values are shown below.

|                           |                                           |
|---------------------------|-------------------------------------------|
| Sodium                    | 142 mEq/L                                 |
| Potassium                 | 3.7 mEq/L                                 |
| Chloride                  | 105 mEq/L                                 |
| Bicarbonate               | 26 mEq/L                                  |
| Blood urea nitrogen       | 28 mg/dL                                  |
| Creatinine                | 1.4 mg/dL                                 |
| TSH                       | 0.1 $\mu$ U/mL                            |
| Brain natriuretic peptide | 640 pg/mL (normal range $\leq 100$ pg/mL) |

Which of the following represents another disease process that can lead to this same presentation?

- (A) Asbestos exposure
- (B) Pulmonary hypertension
- (C) Thiamine deficiency
- (D)  $\alpha_1$ -antitrypsin deficiency
- (E) Sarcoidosis

**The answer is C: Thiamine deficiency.** This patient is presenting with CHF, which is indicated by her symptoms of dyspnea, orthopnea, and paroxysmal nocturnal dyspnea as well as the signs of jugular venous distention, pulmonary edema, and lower-extremity edema. The underlying process leading to this diagnosis is indicated by the review of systems, which suggests hyperthyroidism. Patients with prolonged hyperthyroidism may develop high output cardiac failure, and the question asks for another disease process that can cause this. One answer is thiamine deficiency with the manifestation of wet beriberi. Other causes of high output cardiac failure include anemia, sepsis, large arteriovenous fistulas, and Paget disease. This patient will require treatment for her heart failure as well as treatment of the underlying process of hyperthyroidism.

(A) Asbestos exposure causes pulmonary fibrosis of the lower lobes and increases the risk for squamous cell carcinoma and mesothelioma; it does not commonly cause heart failure. (B) Pulmonary hypertension can lead to heart failure, but this will cause right heart failure without the manifestations of left heart failure (dyspnea from pulmonary edema). (D)  $\alpha_1$ -antitrypsin deficiency causes panacinar emphysema (with physical examination findings of wheezes, not rales) and may also cause liver disease, depending on the genotype. (E) Sarcoidosis can cause a restrictive cardiomyopathy, but does not cause high output cardiac failure.

**26** A 28-year-old man presents to the physician for new onset blurry vision. On examination, his vitals are normal and he appears extremely thin with an arm span much greater than his height, pectus excavatum, and arachnodactyly. On cardiac examination, there is a mid-systolic click at the apex followed by a soft end-systolic murmur.

Which of the following maneuvers will accentuate this murmur?

- (A) Squatting
- (B) Abruptly standing
- (C) Sustained hand grip
- (D) Inspiration

**The answer is B: Abruptly standing.** The patient in this vignette has features of Marfan syndrome, which is caused by an inherited defect in the fibrillin-1 gene. These patients have diffuse connective tissue disease that



affects multiple organs. The chief complaint of this patient is vision loss, which is concerning for lens dislocation (supratemporal dislocation occurs in Marfan syndrome, infranasal in homocystinuria). This disease also affects the leaflets of the mitral valve, producing cystic medial degeneration leading to mitral valve prolapse (MVP). This patient has MVP, which is indicated by the mid-systolic click with mitral regurgitation following prolapse of the leaflet. The clicking sound is thought to be caused by tensing of the chordae tendineae. Patients with Marfan syndrome are also at risk for aortic aneurysm and dissection, especially in the ascending aorta.

The two murmurs that increase upon standing and decrease with squatting should be committed to memory: MVP and hypertrophic cardiomyopathy (HCM). As preload is decreased in the left ventricle during standing, left ventricular volume decreases and the mitral valve leaflet prolapses earlier in systole which leads to a lengthened mitral regurgitation murmur. In HCM, patients have a narrow outflow channel from asymmetric hypertrophy of the interventricular septum. With standing, the decrease in volume further narrows the outflow channel and makes the systolic ejection murmur louder. (A) Squatting will increase both the preload and the afterload, both of which ensure that the left ventricular volume will be increased and thus will reduce the murmur of MVP. (C) The hand grip maneuver will increase systemic vascular resistance and thus increase the afterload seen by the left ventricle, leading to an increase in volume and a decrease in the murmur of MVP. (D) Inspiration leads to a decrease in intrathoracic pressure, increasing preload to the right side of the heart. This increases the flow across the tricuspid and pulmonic valves, accentuating right-sided heart murmurs. Expiration is the opposite process and therefore accentuates left-sided heart murmurs. Inspiration will decrease the murmur of MVP due to a transient decrease in left ventricular preload due to increased volume in the right ventricle as well as an increase in compliance of the pulmonary veins.

27

A 59-year-old man presents with complaints of cough and difficulty breathing. Over the last few days, his dyspnea has progressed to the point where he is short of breath unless resting in a seated position. His cough is nonproductive. He has a history of coronary artery disease and alcoholism. On examination, the patient appears uncomfortable; he is afebrile with a blood pressure of 123/72 mmHg, heart rate of 92 beats per minute, and respiratory rate of 24 breaths per minute. He is obese with a BMI of 36 kg/m<sup>2</sup>. His heart sounds are distant and he has pitting edema of his lower extremities. A bedside ultrasound is of poor quality given the patient's body habitus; however, the inferior vena cava (IVC) is enlarged and the width does not change during the respiratory cycle. A serum ethanol level is negative. His other laboratory tests and chest x-ray (*Figure 1-5*) are shown below.

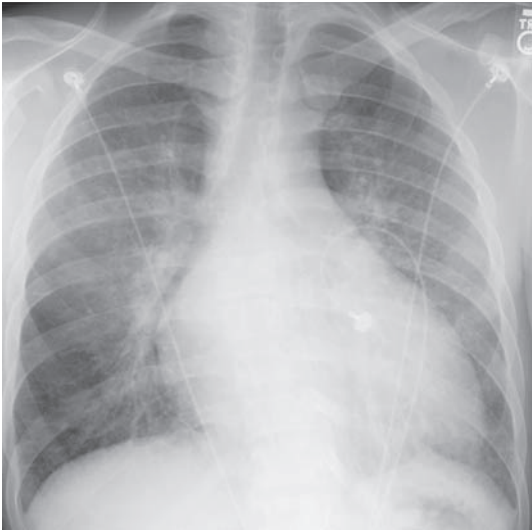


Figure 1-5

|                           |                              |
|---------------------------|------------------------------|
| Hemoglobin                | 16.2 g/dL                    |
| Leukocyte count           | 10,000/mm <sup>3</sup>       |
| Creatinine                | 1.4 mg/dL                    |
| Troponin-I                | Negative                     |
| Brain natriuretic peptide | 96 (normal range ≤100 pg/mL) |

Which of the following is the most likely diagnosis?

- (A) Congestive heart failure
- (B) Nephrotic syndrome
- (C) Pneumonia
- (D) Pericardial effusion

**The answer is A: Congestive heart failure.** The given history is fairly straightforward for CHF, with a description of dyspnea, orthopnea, and a history of coronary artery disease and alcoholism (both of which can contribute to heart failure). A normal ultrasound shows some collapse during inspiration, which is a normal response to decreased intrathoracic pressure. This patient’s IVC is enlarged and fixed during the respiratory cycle, suggesting volume

overload; this is helpful since the jugular venous pulsations may be difficult to appreciate in an obese patient. The chest x-ray shows bilateral pulmonary edema that results from increased hydrostatic pressure in the pulmonary circulation. The one trick to this question is the false-negative brain natriuretic peptide (BNP). BNP is a peptide released primarily by the ventricles in response to increased filling pressures seen in the setting of heart failure. Normally, BNP is extremely sensitive and therefore a negative result pretty much rules out this diagnosis; however, false negatives are reported in obese patients and therefore this diagnosis should still be considered.

(B) Nephrotic syndrome results in edema from loss of intravascular protein in the urine, and so the ultrasound would not show an enlarged IVC. (C) The patient is afebrile, and furthermore pneumonia would not cause pitting edema. (D) A pericardial effusion can also cause an enlarged IVC from increased venous pressures, but would not produce marked pulmonary edema. (On the examination, look for Beck's triad of cardiac tamponade: jugular venous distention, muffled heart sounds, and hypotension.)

28

A 43-year-old woman with systemic lupus erythematosus presents to the hospital with breathlessness and leg swelling. She has been seen by a cardiologist before due to “inflammation of her heart valve,” but she moved out of the city and never received follow-up. On cardiac examination she has an early diastolic opening snap at the apex followed by a diastolic rumbling murmur.

If the opening snap heard during the cardiac examination occurred even closer to the second heart sound, what would this indicate?

- (A) Decreased left ventricular volume
- (B) Decreased left atrial volume
- (C) Increased left ventricular pressure
- (D) Increased left atrial pressure

**The answer is D: Increased left atrial pressure.** Lupus can cause inflammation of the mitral valve, which can progress to mitral stenosis. Rheumatic heart disease is another cause of mitral stenosis and is a result of repetitive exposure to group A strep. This patient is now presenting in heart failure from decompensated mitral stenosis, which should have been diagnosed based on the murmur heard during cardiac examination. In mitral stenosis, there is an obstruction between the left ventricle and the left atrium so that filling of the ventricle during diastole is incomplete. As a result, pressure increases in the left atrium and causes it to become enlarged, which predisposes the patient to atrial fibrillation. The opening snap is an abnormal sound during early diastole that is caused by the thickened mitral valve leaflets opening. Valves only open when there is a change in pressure between two compartments; therefore, the mitral valve will open when the left atrial pressure exceeds left ventricular pressure during diastole (*Figure 1-6*). The higher the left atrial pressure, the

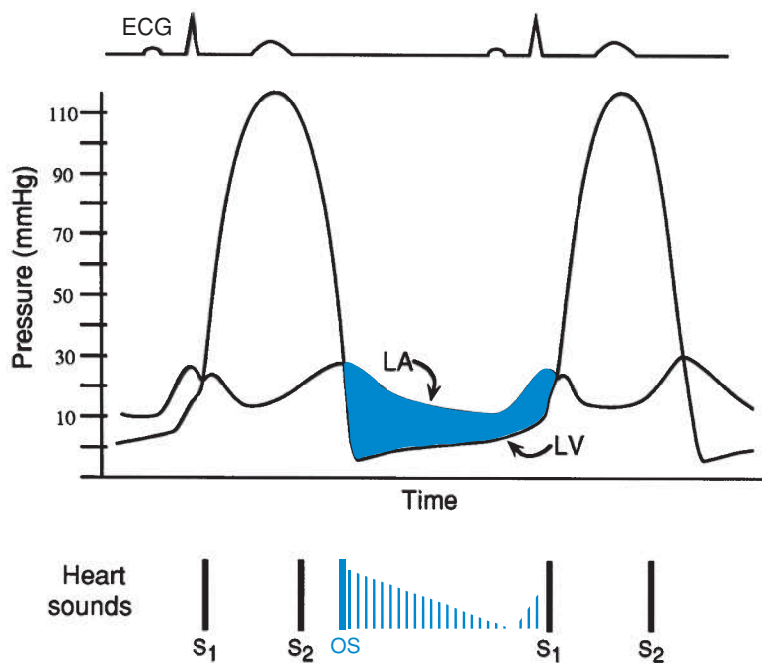


Figure 1-6

earlier the opening snap. Hence the mnemonic “*tight is tight*,” meaning that the more stenotic the valve is (“tight”), the closer the opening snap is to S2 (“tight”). This indicates advanced disease and is a concerning sign. (A, B) Pressure difference between two chambers is the driving force for valve opening/closure, not volume difference. (C) Increased left ventricular pressure would delay the opening of the mitral valve, which is heard as the opening snap.

29

A 34-year-old man with paranoid schizophrenia was brought in by police due to disorganized behavior. He is admitted to the psychiatric ward and undergoes treatment. During hospitalization, the patient becomes unconscious and the following is seen on the monitor (Figure 1-7).

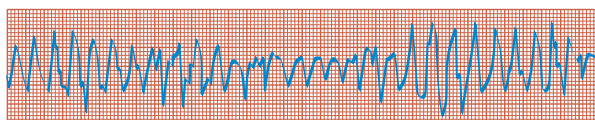


Figure 1-7

Which of the following is the most appropriate initial treatment?

- (A) Magnesium sulfate
- (B) Amiodarone
- (C) Adenosine
- (D) Lidocaine
- (E) Metoprolol

**The answer is A: Magnesium sulfate.** The rhythm shown above is torsades de pointes (“twisting of the points”), a polymorphic ventricular tachycardia which is a feared complication in patients with a prolonged QT interval. In this case, the patient has schizophrenia and therefore is likely on a QT-prolonging antipsychotic medication (such as haloperidol). There are also inherited channelopathies that cause a prolonged QT interval, which are collectively called long QT syndrome. When patients have a prolonged QT interval, they are at risk for the “R on T” phenomenon, which describes depolarization (R of the QRS complex) of the ventricles while many of the myocytes are in the vulnerable relative refractory period (end of the T wave). The result is a potentially fatal arrhythmia. Removal of the offending agent and administering magnesium sulfate is the treatment of choice for torsades. Defibrillation may also be required. (B, C, D, E) The other options are all anti-arrhythmic medications that are not considered to be first-line treatment in this condition.

30

A 58-year-old man comes to your office complaining of occasional chest pain for the past 2 weeks. He was previously active and worked in construction; however, he has had to limit his activity due to the chest pain. The pain occurs with exertion, especially after climbing stairs, and is accompanied by shortness of breath. If he stops to rest, the pain is relieved within 5 minutes. He is not currently experiencing chest pain.

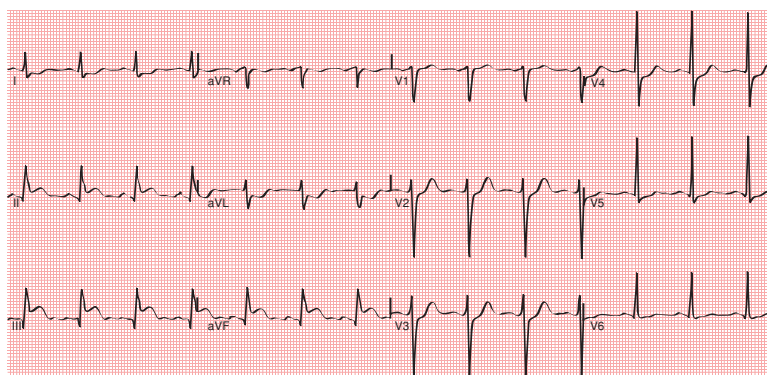
Which of the following is the best next step in management?

- (A) Test his ankle-brachial index (ABI)
- (B) Percutaneous coronary intervention
- (C) Order a stress test
- (D) Administer fibrinolytics
- (E) Reassurance

**The answer is C: Order a stress test.** This patient is likely experiencing stable angina from coronary artery disease. With exertion, the oxygen demand of cardiomyocytes increases but due to fixed atherosclerotic narrowing of the artery, the supply remains constant. This produces a demand–supply mismatch that causes ischemia with anginal chest pain. The next step to make the diagnosis is a stress test. (A) Testing the patient’s ABI would be useful if the patient was presenting with symptoms of claudication from atherosclerosis in

the distal extremities. These symptoms are described as fatigue and cramping of the lower-extremity muscles that resolve with rest. **(B, D)** These would be options if the patient was suffering a myocardial infarction. **(E)** Reassurance would be inappropriate since it is necessary to make the diagnosis and start treatment.

- 31** A 63-year-old man presents with sudden onset retrosternal chest pain that radiates to his jaw and left arm. He has a history of hypertension, hyperlipidemia, and diabetes, but he denies any previous episodes of what he is experiencing now. The patient's ECG is shown below (*Figure 1-8*).

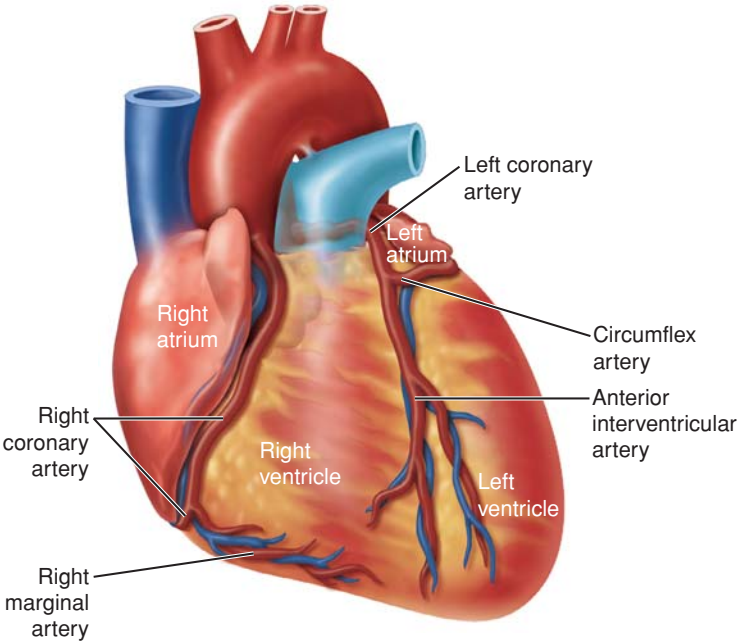


**Figure 1-8**

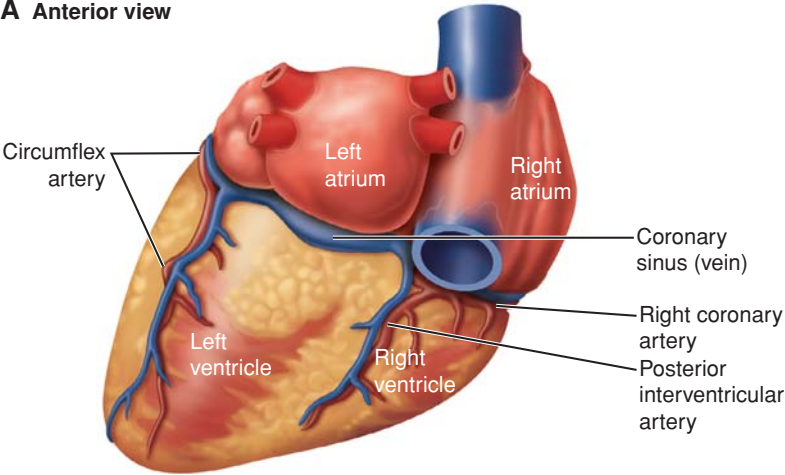
Which coronary artery is most likely affected in this patient?

- (A)** Left anterior descending
- (B)** Left circumflex
- (C)** Right coronary
- (D)** Obtuse marginal

**The answer is C: Right coronary.** There are ST elevations in II, III, and aVF, indicating an inferior STEMI. Either the right coronary artery or the left circumflex artery supply this region of the heart. However, 80% of people are “right-dominant” and have the posterior descending artery originating off the right coronary artery to supply the inferior region of the heart. It is important to know the vascular anatomy of the heart and how to assess the likely vascular territory affected based on an ECG. This information is summarized in *Table 1-1* and *Figure 1-9*.



**A** Anterior view



**B** Posterior view

**Figure 1-9**

**Table 1-1 ECG Findings in Myocardial Infarction**

| MI Location  | Affected Artery  | Leads                      |
|--------------|------------------|----------------------------|
| Anteroseptal | LAD              | V1–V4                      |
| Apical       | LAD, LCx, or RCA | V5–V6                      |
| Lateral      | LCx              | I, aVL                     |
| Inferior     | RCA > LCx        | II, III, aVF               |
| Posterior    | RCA or LCx       | ST depressions V1–V3       |
| RV infarct   | RCA              | V1–V2, V4R (reverse leads) |

**32**

A 69-year-old woman with a history of hypertension, diabetes, and myocardial infarction comes to the hospital with worsening shortness of breath and leg swelling. She has an S3 on examination with crackles at both lung bases and 2+ pitting edema in her lower extremities. The level of brain natriuretic peptide is elevated and a chest x-ray shows vascular congestion with bilateral fluffy opacities.

Which of the following would be unlikely to contribute to the patient's current presentation?

- (A) Excessive sodium in the diet
- (B) Forgetting to take medications
- (C) Digoxin
- (D) Naproxen
- (E) Renal failure

**The answer is C: Digoxin.** Digoxin is a cardiac glycoside that functions as an inotropic agent, working to increase the contractility of the heart and therefore the cardiac output. It does this by blocking the sodium–potassium pump, leading to an increased concentration of sodium ions within myocytes and subsequently an increase in intracellular calcium through the sodium–calcium exchanger. Increased intracellular calcium leads to an increased contractility of the heart. Digoxin may be used to reduce symptoms of heart failure and hospitalization rates; however, it does not decrease mortality. Important side effects include atrial tachycardia with AV block, vision changes (yellow vision), and gynecomastia. Other drug causes of gynecomastia may be remembered with the mnemonic “*Some Drugs Create Awesome Knockers*.” Spironolactone, Digoxin, Cimetidine, Alcohol, Ketoconazole.

(A, B) Medication and dietary noncompliance are common precipitants of acute heart failure. (D) Naproxen is an NSAID, and NSAIDs as a class may also precipitate heart failure; other etiologic medications include  $\beta$ -blockers and



calcium channel blockers. Note that  $\beta$ -blockers and calcium channel blockers may be beneficial in heart disease, but they may also contribute to heart failure if used in excess or in the setting of other precipitants of heart failure. (E) Renal failure leads to an increase in intravascular volume, which is delivered to a failing heart that already struggles to move blood forward.

33

A 58-year-old man presents to the hospital with persistent fatigue and some exertional dyspnea. He has a history of hypertension, diabetes, and atrial fibrillation. Cardioversion was attempted previously but without success. He was lost to follow-up, but reports that he takes lisinopril and metformin regularly. On examination, he is normotensive with a heart rate of 76 beats per minute with an irregularly irregular rhythm. There are no murmurs or extra heart sounds, and his lungs are clear to auscultation bilaterally.

Which of the following is the most appropriate next step in management?

- (A) Repeat cardioversion
- (B) Aspirin
- (C) Warfarin
- (D) Amiodarone

**The answer is C: Warfarin.** This question is testing the reader's understanding of appropriate prophylactic anticoagulation to prevent thromboembolic events. Decision about which agent to use should be guided by the patient CHADS<sub>2</sub> score: 1 point for CHF, Hypertension, Age >75, and Diabetes; 2 points for previous Stroke or transient ischemic attack (TIA). For a score of 0, aspirin should be started; for a score of 1, aspirin or warfarin should be started; and for a score  $\geq 2$ , warfarin should be started. This patient has hypertension and diabetes, giving him a CHADS<sub>2</sub> score of 2, and therefore warfarin is the most appropriate therapy to reduce the patient's risk of stroke.

(A) This patient has chronic atrial fibrillation, and repeat cardioversion may be attempted (since the patient is symptomatic) but only after sufficient anticoagulation. (B) Aspirin would only be appropriate if the patient's CHADS<sub>2</sub> score was 0 or 1. (D) Rate control is equivalent to rhythm control in chronic atrial fibrillation and has less side effects and is therefore preferred. Amiodarone can be used for rate control but is unpopular for two reasons: there are many side effects, and amiodarone is an anti-arrhythmic that may induce chemical cardioversion and cause embolization of a clot in the left atrium.

34

A 48-year-old man is hospitalized with shortness of breath and ascites. Over the past 8 years, he reports that he experienced symptoms of severe fatigue, painful joints, and a decreased interest in sex. He never saw a physician during this time due to an inability to obtain medical insurance. More recently, he developed severe dyspnea on exertion

with swelling of his abdomen and legs. He has no medical history and takes no medications. His uncle died from liver disease. He drinks 10 to 12 beers weekly and has never smoked. On examination, he has scleral icterus with no lymphadenopathy. There is jugular venous distention and a laterally displaced PMI. He has bilateral wet rales on lung auscultation. There is no appreciable hepatomegaly, but there is flank dullness with a fluid wave on abdominal examination. He has 2+ pitting edema of his lower extremities bilaterally. Skin findings include diffusely darkened skin, spider angiomas on the chest, and palmar erythema. His laboratory values are shown below.

|                            |                               |
|----------------------------|-------------------------------|
| Leukocyte count            | 7,000/mm <sup>3</sup>         |
| Platelets                  | 124,000/mm <sup>3</sup>       |
| Creatinine                 | 1.6 mg/dL                     |
| Glucose                    | 235 mg/dL                     |
| Albumin                    | 2.5 g/dL                      |
| Total bilirubin            | 5.4 mg/dL                     |
| Aspartate aminotransferase | 54 U/L                        |
| Alanine aminotransferase   | 30 U/L                        |
| Alkaline phosphatase       | 92 U/L                        |
| INR                        | 1.8                           |
| Brain natriuretic peptide  | 540 (normal range ≤100 pg/mL) |

Which of the following could have prevented this patient's current manifestations?

- (A) Methotrexate
- (B) Alcohol cessation
- (C) Regular phlebotomy
- (D) Penicillamine

**The answer is C: Regular phlebotomy.** There are a constellation of findings in this patient that suggest the diagnosis of hemochromatosis: darkened skin, diabetes mellitus, advanced liver disease (elevated bilirubin and INR, low albumin, thrombocytopenia), heart failure (displaced PMI, elevated BNP), and a family history of liver disease. Hemochromatosis is an autosomal recessive disease caused by a mutation in the HFE gene leading to unregulated iron

absorption and overload. It presents in males after the age of 40, but will present later in females due to blood loss during menstruation. Early symptoms include fatigue, arthritis, and a decreased libido. If the disease is not recognized early, iron deposition can affect many organs including the liver (primary organ affected), pancreas, and heart, leading to the manifestations seen in this patient (cirrhosis, diabetes, and dilated cardiomyopathy). Because there is no physiologic mechanism to excrete large amounts of iron, the treatment of this condition is phlebotomy on a regular basis.

(A) Methotrexate is a dihydrofolate reductase inhibitor used in the treatment of various cancers and autoimmune conditions. It is a disease-modifying antirheumatic drug (DMARD) that has been successful in the treatment of rheumatoid arthritis, but it would not be helpful here. (B) This patient drinks less than two drinks per day on average, which is within the category of moderate alcohol consumption. Though drinking alcohol is not recommended in the presence of liver disease, alcohol cessation would not prevent the progression of hemochromatosis. (D) Penicillamine is a copper chelator used in the treatment of Wilson disease. Iron chelators (e.g., deferoxamine) can be used in hemochromatosis only if the patient is not willing to undergo regular phlebotomy.

35

A 48-year-old woman presents to the Emergency Department with ascites and leg swelling. Your attending tells you that the patient has a history of idiopathic pulmonary fibrosis (IPF) and is now presenting with acute heart failure. The patient is at her baseline respiratory status; there is jugular venous distention, a 2/6 holosystolic murmur heard at the left lower sternal border that increases with inspiration, and a right-sided S4. Lung sounds are distant, with scattered wheezes but no rales. The attending asks you what caused this patient's presentation.

Which of the following best represents the initial pathologic process that led to this patient's heart failure?

- (A) Calcification of the aortic valve
- (B) Increased pulmonary artery pressure
- (C) Infiltration of the myocardium
- (D) Fibrosis of the pericardium

**The answer is B: Increased pulmonary artery pressure.** The key here is recognizing that the patient is presenting with symptoms of right heart failure, not left heart failure. Although the most common cause of right heart failure is left heart failure, there are additional processes that may produce isolated right heart failure. Cor pulmonale is the term given to right heart failure that results from pulmonary hypertension associated with a primary pulmonary disease. Destructive lung processes will cause a loss of pulmonary vasculature, requiring that the same amount of blood volume be pumped through fewer arterioles. In addition, hypoxia from destruction of lung parenchyma will lead to hypoxic vasoconstriction, which is the lung's mechanism

for reducing ventilation–perfusion mismatch with regional hypoxia. Both of these mechanisms contribute to increased pressure in the pulmonary artery, known as pulmonary hypertension. This will lead to increased pressure load on the right ventricle, eventually leading to right heart failure that spares the distal left ventricle. Therefore, the best answer choice here is increased pulmonary artery pressure.

(A) Calcification of the aortic valve is known as senile aortic stenosis; if untreated, it results in left heart failure. (C) Certain infiltrative processes (sarcoidosis, amyloidosis, hemochromatosis) may cause heart failure by producing a restrictive cardiomyopathy which reduces the compliance of the ventricles. This would produce both left and right heart failure. (D) Fibrosis of the pericardium refers to constrictive pericarditis, which can occur as a consequence of any cause of pericarditis (viral, uremia, radiation, TB, etc.). With this diagnosis, look for Kussmaul sign on examination (paradoxical increase in jugular venous pressure during inspiration).

**36** A 32-year-old woman with a history of HIV presents to the hospital with severe shortness of breath. She completed her last round of chemotherapy for non-Hodgkin lymphoma 6 months ago, and has since been in remission. She is afebrile and normotensive, but has a respiratory rate of 28 breaths per minute. She has an S3 on examination with distended neck veins and wet rales at the bases of her lungs. A chest x-ray shows bilateral opacities with air bronchograms and small pleural effusions.

Which of the following is the most appropriate next step in management?

- (A) Piperacillin/tazobactam and vancomycin
- (B) Prednisone then trimethoprim/sulfamethoxazole
- (C) Percutaneous coronary intervention
- (D) IV furosemide

**The answer is D: IV furosemide.** The question asks for the management of acute heart failure, but there are a couple of quick teaching points. First, the patient is HIV+ and therefore is at risk for opportunistic infections (OIs) as well as some cancers (including lymphoma, which occurred in this patient). Second, anthracycline chemotherapy (doxorubicin, daunorubicin) is commonly given for treatment of non-Hodgkin lymphoma (part of CHOP or R-CHOP therapy); a high-yield adverse effect of these drugs is cardiotoxicity, which can result in heart failure. This patient is presenting with findings of acute heart failure, and the management of this condition can be remembered using the mnemonic *LMNOP* (Lasix, Morphine, Nitrates, Oxygen, Position). These patients require diuresis with IV loop diuretics to remove excess fluid, which will reduce excessive filling pressures and improve the cardiac output of the heart.

(A) Although pneumonia may be considered in the differential, the physical examination findings (especially jugular venous distention) is more consistent with heart failure. The fact that she is afebrile does not rule out infection, since HIV patients often do not mount an appropriate immune response to infections. (B) PCP pneumonia is a common OI in patients with HIV, and treatment with prednisone prior to trimethoprim-sulfamethoxazole is warranted with severe infections. (C) Although myocardial infarction can cause heart failure, there is nothing in the question stem to suggest this as the cause. In addition, PCI would only be appropriate after other tests are performed to confirm the diagnosis (ECG, troponins, etc.).

37

A 38-year-old man with no medical history presents to the hospital with worsening shortness of breath. He reports that the symptoms are worse while lying down and in certain positions. On examination, he is afebrile with a normal blood pressure. A mid-diastolic murmur is heard at the apex and there is a plopping noise heard during early diastole. The nature of the murmur changes with body positioning. An echocardiogram is performed which shows a mass arising from the left atrium.

Which of the following is the most likely diagnosis?

- (A) Left atrial thrombus
- (B) Infective endocarditis
- (C) Atrial sarcoma
- (D) Atrial myxoma

**The answer is D: Atrial myxoma.** Although tumors of the heart are rare, a murmur similar to mitral stenosis that changes with position and is associated with a plopping noise should raise a concern for this diagnosis. Atrial myxomas are the most common primary cardiac tumors and are benign. Surgery is required to remove the mass and prevent complications such as obstructive shock and tumor emboli. Metastases to the heart are more common than primary cardiac tumors, and melanoma is a cancer that can metastasize here (always think of melanoma as metastasizing to strange locations); however, this was not provided as an answer choice. (A) The echocardiogram described a mass arising from the atrium, and on examination there was a characteristic “tumor plop” sound as the tumor falls back in place during diastole. A thrombus would not present with cause these findings. (B) The patient is afebrile and does not meet the modified Duke criteria, making infective endocarditis less likely. (C) Atrial sarcomas are malignant cardiac tumors; however, they are not the most common primary cardiac tumor.

38

A 62-year-old man presents to the Emergency Department with difficulty breathing. The dyspnea began acutely earlier in the day without any trigger, and was accompanied by nausea and sweating. He denies any fevers, chest pain, abdominal pain, or frequent urination. He has

a long history of type 2 diabetes mellitus, hypertension, and diabetic neuropathy, for which he takes metformin, lisinopril, and gabapentin, respectively. His vitals are taken and he is afebrile with a blood pressure of 98/60 mmHg, heart rate of 111 beats per minute, respiratory rate of 30 breaths per minute, and oxygen saturation of 94% on room air. He is extremely uncomfortable and short of breath during examination. His neck veins are distended with no cardiac murmurs auscultated. Rales are heard over both lung bases. When pressure is applied to his upper abdomen, the neck veins distend further and return to baseline after 15 seconds. Initial laboratory values are shown below.

|                         |                         |
|-------------------------|-------------------------|
| Hemoglobin              | 13.5 g/dL               |
| Leukocyte count         | 10,500/mm <sup>3</sup>  |
| Platelets               | 350,000/mm <sup>3</sup> |
| Bicarbonate             | 22 mEq/L                |
| Creatinine              | 1.6 mg/dL               |
| Glucose                 | 193 mg/dL               |
| Urinalysis              | 1+ protein              |
| Urine toxicology screen | Negative                |

Which of the following is the most appropriate first order to make?

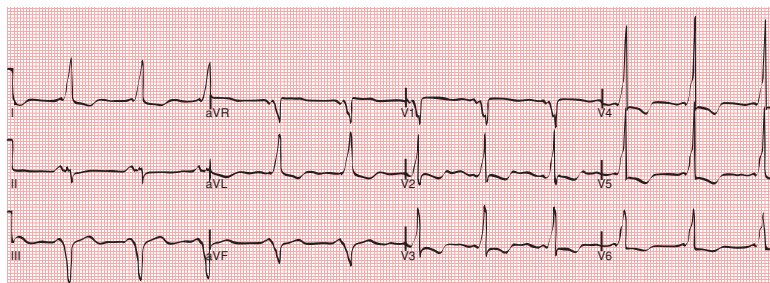
- (A) Chest x-ray
- (B) Order urine and serum ketones
- (C) CT angiogram
- (D) Blood, urine, and sputum cultures
- (E) Troponins and an ECG
- (F) IV fluid bolus

**The answer is E: Troponins and an ECG.** This is a diabetic patient presenting with evidence of end-organ damage from this disease. He has an elevated creatinine and proteinuria, with a history of neuropathy. In patients with diabetic neuropathy, innervation to the heart may also be affected and these patients can have myocardial infarctions without chest pain. Because diabetes and hypertension are risk factors for cardiovascular events, it is important to have a very low index of suspicion for ACS in these patients. The sudden onset of symptoms and findings of cardiac failure on examination (distended neck veins, positive abdominojugular reflex) make ACS a concern. Therefore, the next step should be to order troponins and an ECG.

(A) A chest x-ray would not add much additional information at this point other than to confirm the presence of pulmonary edema. (B) Urine and serum ketones would assess for diabetic ketoacidosis; however, there are no other historical or examination findings to suggest this as a likely diagnosis; the acute onset of symptoms also argue against this. (C) Although pulmonary embolism could present like this and certainly should be on the differential, a CT angiogram contains contrast and therefore should not be ordered immediately given that the patient has evidence of renal failure. A V/Q scan would be more appropriate in this case. (D) An infection is unlikely since the patient is afebrile with a normal white count. (F) Excessive IV fluids may harm the patient, since the patient's hypotension is cardiogenic in nature and not due to hypovolemia (distended neck veins).

39

A 26-year-old woman presents to the Emergency Department after fainting. She is a graduate student and reports staying up all night to finish a paper and drinking several energy drinks. While sitting at her desk, she felt her heart racing and then lost consciousness. She awoke without any memory loss but is concerned that it will happen again. She currently has a normal heart rate and blood pressure. Her ECG is shown in *Figure 1-10*.



**Figure 1-10**

Which of the following agents should be avoided while the patient is in the Emergency Department?

- (A) Metoprolol
- (B) Flecainide
- (C) Propafenone
- (D) Amiodarone

**The answer is A: Metoprolol.** The ECG shows the classic delta waves and short PR interval of Wolff-Parkinson-White (WPW) syndrome, which is caused by an accessory pathway that bypasses the AV node and can cause serious tachyarrhythmias. The gradual upslope of the QRS complexes (delta waves) are caused by early depolarization of the ventricles through the accessory pathway. Asymptomatic patients do not require treatment; however,

this patient experienced syncope and thus deserves treatment to prevent further episodes. Catheter ablation of the accessory pathway should be offered to symptomatic patients, since there are high success rates without the need for chronic medications.  $\beta$ -blockers, calcium channel blockers, and digoxin are contraindicated in WPW since they slow down conduction through the AV node and thus can facilitate conduction down the accessory pathway and precipitate a life-threatening tachyarrhythmia. (An important caveat is that these agents may be used during an acute tachyarrhythmia to stop conduction through the AV node, terminating the reentrant tachycardia.)

(B, C) If catheter ablation is refused, then the first-line choice for a chronic prophylactic agent is a class IC anti-arrhythmic (e.g., flecainide, propafenone). (D) Amiodarone is an alternative to class IC anti-arrhythmics for chronic prophylaxis.



An elderly man is hospitalized for chest pain and requires cardiac catheterization with placement of a stent. He recovers and is discharged. One month later, he presents to your clinic with a 1-week history of fever and stabbing chest pain. His vitals are within normal limits, and there is a scratching noise that is best heard at the left lower sternal border.

What is the most appropriate treatment at this time?

- (A) Conservative management
- (B) Ibuprofen
- (C) Ceftriaxone, levofloxacin, and vancomycin
- (D) Azithromycin
- (E) Prednisone

**The answer is B: Ibuprofen.** This patient is presenting with Dressler syndrome, which is a self-limited autoimmune pericarditis that typically occurs 2 to 10 weeks after a myocardial infarction. It presents like acute pericarditis (pleuritic chest pain relieved by leaning forward), and the treatment is NSAIDs. The scratching noise heard during physical examination is a friction rub, which typically has three parts and is caused by inflamed pericardium rubbing together during cardiac motion.

(E) Prednisone is not necessary in these patients. (C, D) The antibiotic regimens are for community-acquired pneumonia (azithromycin) and health care-associated pneumonia (ceftriaxone, levofloxacin, and vancomycin); although it may be tempting to consider pneumonia in a patient presenting with fever and chest pain, the association with a recent myocardial infarction should lead the reader to suspect one of the postmyocardial infarction complications rather than pneumonia.



A 62-year-old Caucasian man presents to the clinic for his annual physical examination. The patient has a history of hypertension, which is adequately controlled with medications and lifestyle changes. The



patient reluctantly admits that he still smokes a half pack of cigarettes daily. On examination, his blood pressure is 132/88 mmHg. During the physical examination, a pulsatile abdominal mass is noted. The patient denies any symptoms from the mass. An ultrasound is ordered and reveals that the abdominal aortic diameter is 4.5 cm.

What is the next step in management?

- (A) Observation
- (B) Rapid reduction in blood pressure
- (C) Immediate surgery
- (D) Surgery within the next 48 hours

**The answer is A: Observation.** Although abdominal aortic aneurysms (AAAs) are potentially fatal, the best evidence argues for conservative management when the aneurysm is <5.5 cm in diameter. There are some modifications to this rule based on other patient factors (e.g., patients with Marfan syndrome); however, this is a good general number to remember. These patients can be followed with serial imaging every 6 to 12 months with ultrasound or CT. Risk factors for AAAs include increasing age, male gender, Caucasian race, atherosclerosis, and most importantly smoking. Smoking cessation is the most important immediate intervention for this patient to reduce the rate of growth and the risk of rupture. In addition, he should start aspirin and a statin since an AAA is a coronary artery disease risk equivalent (others are diabetes, carotid artery disease, and peripheral vascular disease). Asymptomatic AAAs may be diagnosed on physical examination or screening (USPSTF recommends a one-time ultrasound in males aged 65 to 75 with a history of smoking). AAAs are usually not symptomatic but can present with abdominal or back pain and limb ischemia. In a patient with abdominal pain, distention, and hemodynamic instability, always consider rupture of an AAA.

(B) Blood pressure control with  $\beta$ -blockers and ACE inhibitors may decrease the rate of growth and risk of rupture; however, this patient's blood pressure is at goal (<150/90 mmHg as per the most recent guidelines). Rapid reduction in blood pressure is important for patients with type B aortic dissections (involving the descending aorta); type A dissections (involving the ascending aorta) require immediate surgery. (C, D) This patient has an asymptomatic AAA <5.5 cm and therefore does not require surgery at this time.



A 68-year-old woman presents to the Emergency Department with substernal chest pain radiating to her jaw. Her medical history is significant for hypertension and hyperlipidemia. Troponins are positive, and an ECG confirms STEMI. She undergoes percutaneous coronary intervention. The rest of her hospitalization is unremarkable, and she is eventually discharged. She returns to your office 1 month later complaining of a persistent dry cough without any other symptoms. Physical examination is unremarkable.

Which of the following is the most appropriate next step in management?

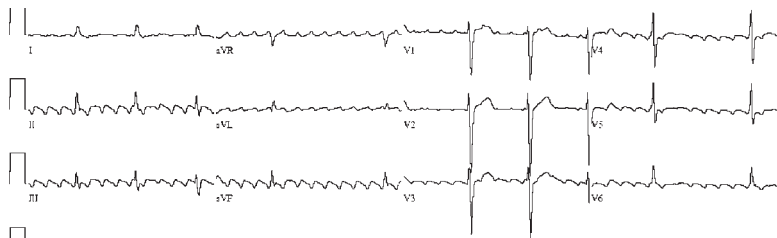
- (A) Check troponin levels and refer for stress test
- (B) Stop the patient's lisinopril and start losartan
- (C) Order a chest x-ray
- (D) Stop the patient's aspirin and start bronchodilator therapy
- (E) Reassurance

**The answer is B: Stop the patient's lisinopril and start losartan.** This is a two-part question, which tests the reader's knowledge of (1) appropriate discharge medications after a myocardial infarction and (2) the important adverse effects of these medications. After an MI, all patients should be discharged on the following medications: aspirin, clopidogrel,  $\beta$ -blocker, ACE inhibitor or angiotensin receptor blocker (ARB), and statin. ACE inhibitors and ARBs improve mortality postmyocardial infarction by reducing blood pressure as well as harmful cardiac remodeling (note: ACE inhibitors and ARBs should not be used together). The most likely cause of the patient's cough at this time is an adverse effect from the ACE inhibitor. ACE inhibits the conversion of angiotensin I to angiotensin II, which occurs primarily in the lungs. It also inactivates bradykinin, so ACE inhibition leads to the build up of bradykinin in the lungs which is responsible for the dry cough.

(A, C) Given that the patient is presenting without any other symptoms or any concerning physical examination findings, checking troponin levels and ordering a chest x-ray are unnecessary at this time. (E) Although reassurance is commonly a correct answer when seen on the shelf examination, it is inappropriate to reassure the patient if the cough is a bothersome symptom. (D) Aspirin allergy is not a true "allergy" and would not present like this; for the shelf examination, look for the classic triad of a patient with asthma, chronic rhinosinusitis with nasal polyps, and taking aspirin or other NSAIDs.

43

A 63-year-old woman presents to the hospital with shortness of breath and palpitations that started this morning. She has a history of coronary artery disease and takes appropriate medications. Her ECG is shown below (*Figure 1-11*).



**Figure 1-11**

Which of the following is the most likely diagnosis?

- (A) Atrial fibrillation
- (B) Atrial flutter
- (C) Multifocal atrial tachycardia
- (D) Atrioventricular nodal reentrant tachycardia (AVNRT)

**The answer is B: Atrial flutter.** The rhythm of atrial flutter can be diagnosed on ECG by the classic “sawtooth” pattern, which is best seen in the inferior leads (II, III, aVF). It is typically caused by a premature atrial impulse that leads to a self-perpetuating loop around the tricuspid annulus. One tip-off on an ECG is an atrial rate of 300 beats per minute with a 2:1 conduction ratio through the AV node, leading to a heart rate of 150 beats per minute.

(A) Atrial fibrillation would show an irregularly irregular rhythm on ECG with no identifiable P waves. (C) Multifocal atrial tachycardia is a rarely tested supraventricular tachycardia that is caused by multiple ectopic foci in the atria; P waves of various morphology are seen on ECG. (D) AVNRT and AV reciprocating tachycardia (AVRT) involve re-entrant circuits in either the AV node solely (AVNRT) or in the AV node with an accessory pathway (AVRT). They typically cause a heart rate >150 beats per minute with P waves that are buried within the QRS complexes.

44

A 59-year-old man with a history of nonischemic cardiomyopathy presents to the hospital with leg swelling and extreme shortness of breath. He reports that several weeks ago, he had trouble obtaining his medications due to losing his medical insurance. He normally takes losartan, carvedilol, nifedipine, aspirin, furosemide, atorvastatin, insulin, and omeprazole. His vitals show a blood pressure of 104/64 mmHg, a heart rate of 72 beats per minute, and a respiratory rate of 28 breaths per minute. He has an S3 on examination with bilateral rales at his lung bases and 2+ pitting edema of his lower extremities up to his sacrum. An ECG shows no acute ST elevations or depressions. A chest x-ray shows bilateral fluffy opacities, and an echocardiogram shows an estimated ejection fraction of 20%.

Which of the following medications should not be resumed at this time?

- (A) Furosemide
- (B) Insulin
- (C) Losartan
- (D) Atorvastatin
- (E) Carvedilol
- (F) Nifedipine

**The answer is E: Carvedilol.** In the setting of acute decompensated heart failure, a patient's dosage of  $\beta$ -blocker should be reduced or discontinued based on the severity of symptoms. This is done to help improve the rate and contractility of the heart in order to improve symptoms and aid in diuresis. (A) Furosemide should be continued, but it should be switched to IV administration in order to aggressively diurese this patient. (C) The patient's ARB should be held if he becomes hypotensive; however, it may be continued at this time. (B, D, F) The rest of the medications can be resumed safely.



45 A 55-year-old man presents to the hospital with progressive dyspnea over the course of the last few weeks. He denies fever, cough, or chest pain. He has no significant medical or family history, but endorses drinking two 750-mL bottles of wine daily. He is afebrile with a blood pressure of 139/82 mmHg, heart rate of 98 beats per minute, and respiratory rate of 24 breaths per minute. The point of maximal impulse is displaced laterally, a 2/6 holosystolic murmur is heard at the apex, and an S3 is auscultated. There are crackles at the lung bases with pitting edema around the ankles.

Which of the following is the most important intervention for this patient?

- (A) Low sodium diet
- (B) Cardiac glycoside
- (C)  $\beta$ -blocker
- (D) Alcohol cessation

**The answer is D: Alcohol cessation.** The patient in this vignette is presenting with symptoms and signs of heart failure from a dilated cardiomyopathy. There are many causes of dilated cardiomyopathy, but the significant history of heavy alcohol intake points to this as the underlying cause. Alcohol is directly toxic to cardiomyocytes and can cause left ventricular dysfunction with subsequent cardiac dilation. The most important first step with toxic cardiomyopathies is to stop the offending agent. If abstinence is initiated immediately, the condition may be reversible with return of normal left ventricular function. Without abstinence, these patients will continue to progress to heart failure and require the medications and devices appropriate for heart failure of any cause. Other important causes of dilated cardiomyopathy include ischemic heart disease, myocarditis (Coxsackie viruses, HIV, Lyme disease, Chagas disease, etc.), chronic valvular disease, stress-induced (Takotsubo cardiomyopathy) or chronic tachycardia, and certain metabolic conditions (hypothyroidism, pheochromocytoma, etc.). Besides alcohol, other toxins that can cause a dilated cardiomyopathy include cocaine and anthracycline chemotherapy. (A, B, C) These interventions and medications

are potentially helpful in heart failure; however, the patient has a potentially reversible cause of heart failure and therefore cessation of the offending agent is the best option.

46

A 47-year-old man presents to the clinic complaining of leg swelling. He has a long history of hypertension and diabetes, with a recent change in his medications, although he cannot remember the names of the new drugs. He has no other complaints, and he denies any shortness of breath or orthopnea. His physical examination, other than bilateral edema of the lower extremities, is completely normal.

Which medication is most likely responsible for the patient's complaint?

- (A) Amlodipine
- (B) Metoprolol
- (C) Hydrochlorothiazide
- (D) Metformin
- (E) Glipizide

**The answer is A: Amlodipine.** Amlodipine is a calcium channel blocker that is often used as an antihypertensive agent. It has a high incidence of peripheral edema as a side effect. (B) Metoprolol is a selective  $\beta_1$  blocker used in hypertension, heart failure, and rate control for atrial fibrillation. It can cause bradycardia and hypotension, but avoids some of the adverse effects of nonselective  $\beta$ -blockers (e.g., bronchospasm). It rarely causes peripheral edema. (C) Hydrochlorothiazide blocks the Na-Cl channel in the distal convoluted tubule, leading to sodium and water excretion. It is used as an antihypertensive agent, and can cause orthostatic hypotension, hypercalcemia, hypokalemia, hyperlipidemia, and hyperglycemia. (D) Metformin is a biguanide drug used in diabetes and acts by decreasing hepatic glucose secretion and increasing insulin sensitivity. It causes GI symptoms, vitamin B<sub>12</sub> deficiency, and lactic acidosis in patients with renal failure. (E) Glipizide is a sulfonylurea antidiabetic drug. It blocks potassium channels in islet cells of the pancreas, leading to increased insulin release that can result in hypoglycemia.

47

A 22-year-old volleyball player comes to your clinic after a syncopal episode during a game. She is in good health and has no other medical problems. Her family is healthy, although she has an uncle that died for unknown reasons at the age of 32. On examination, there is a 2/6 systolic ejection murmur at the left sternal border that becomes louder during a Valsalva maneuver.

Which of the following is the most appropriate next step in management?

- (A) Electrophysiology study
- (B) Echocardiogram
- (C) Tilt table test
- (D) Reassurance

**The answer is B: Echocardiogram.** This patient is a young athlete who experienced syncope during exertion. She has a systolic ejection murmur and a family history of sudden death, raising a suspicion for hypertrophic cardiomyopathy (HCM). HCM is an autosomal dominant disease that causes myocardial hypertrophy involving the septum leading to left ventricular outflow obstruction. Patients can present with dyspnea, chest pain, syncope, or arrhythmias, which may present during physical activity when there is increased cardiac contractility, decreased preload, and decreased afterload, all of which reduce left ventricular volume and worsen the outflow obstruction. Patients may require  $\beta$ -blockers or calcium channel blockers to decrease heart rate and contractility; other options include surgical myectomy or septal ablation. Patients may also require an implantable cardioverter-defibrillator (ICD) to prevent life-threatening arrhythmias. An echocardiogram is the next step in managing this patient to make the diagnosis and assess the degree of outflow obstruction.

(A) This patient has a murmur on examination, indicating a structural heart defect and not necessarily an electrical problem. Though arrhythmias are common in hypertrophic cardiomyopathy, there is no reason to perform an electrophysiology study at this time. (C) A tilt table test can be used to diagnose vasovagal (neurocardiogenic) syncope; however, HCM is the more likely and concerning diagnosis. (D) The patient should refrain from heavy physical exertion and stay adequately hydrated to maintain preload. This is not a benign process and reassurance is not appropriate.

**48** A 29-year-old woman presents to the hospital with a 3-day history of fever, night sweats, cough, and dyspnea. Her cough is productive of yellowish sputum. She denies ever having these symptoms in the past, and has no recent exposures to sick contacts. She has no significant medical history and takes no medications. She smokes 5 to 7 cigarettes daily, drinks alcohol socially, and admits to occasional illicit drug use. On examination, her temperature is 38.6°C, blood pressure is 124/76 mmHg, heart rate is 95 beats per minute, respiratory rate is 24 breaths per minute, and oxygen saturation is 97%. There is a 3/6 holosystolic murmur at the left sternal border that increases in intensity during inspiration. Her liver is enlarged and pulsatile. Some scarring and needle track marks are seen in the antecubital fossa, but there are no other skin findings and her

neurologic examination is normal. Her laboratory values and chest x-ray (Figure 1-12) are shown below.

|                     |                         |
|---------------------|-------------------------|
| Leukocyte count     | 14,500/mm <sup>3</sup>  |
| Platelets           | 375,000/mm <sup>3</sup> |
| Blood urea nitrogen | 22 mg/dL                |
| Creatinine          | 1.0 mg/dL               |



**Figure 1-12**

Which of the following is the most likely diagnosis?

- (A) Community-acquired pneumonia
- (B) PCP pneumonia
- (C) Infective endocarditis
- (D) Tuberculosis
- (E) Rheumatic fever
- (F) Pulmonary embolism

**The answer is C: Infective endocarditis.** This patient presented with a constellation of findings that meet criteria for acute bacterial endocarditis, which is most likely caused by *S. aureus* in IV drug users like this patient. Diagnosis is based on the modified Duke criteria, in which the definitive diagnosis is made with any of the following criteria: two major, one major and three minor, or five minor. Major criteria include bacteremia (confirmed with blood culture) of an organism known to cause endocarditis and valve involvement (new regurgitant murmur or vegetation on echocardiogram). Minor criteria include predisposing conditions (e.g., IV drug use), fever, vascular phenomena

(e.g., pulmonary emboli, Janeway lesions), immune phenomena (e.g., Osler nodes), and positive blood cultures that do not meet major criteria. This patient has one major criterion (tricuspid regurgitation) and three minor criteria (IV drug use, fever, and pulmonary emboli). Her tricuspid regurgitation is indicated by the murmur on examination and the pulsatile liver, which is virtually diagnostic of tricuspid regurgitation. There are no skin findings or renal involvement in this patient since her disease is limited to the tricuspid valve with emboli to the lungs. Cultures should be obtained and then empiric IV antibiotics should be started.

(A, B, D) Another infectious process may be considered given her symptoms and risk factors; however, the murmur on examination with the chest x-ray showing embolic events is much more concerning for endocarditis. PCP pneumonia will usually show diffuse interstitial infiltrates on chest x-ray. (E) Rheumatic fever is an autoimmune complication of untreated Group A Strep infection, and it typically presents with additional symptoms including arthralgias, skin rash, and chorea. It is diagnosed using Jones criteria. (F) Pulmonary embolism would show a normal x-ray or subtle findings such as pulmonary vascular congestion with wedge-shaped infarcts.

**49** A 72-year-old woman presents to the Emergency Department with chest pain and shortness of breath. She has a blood pressure of 124/73 mmHg, and on cardiac examination she has a blowing holosystolic murmur at the apex that radiates to her axilla. Her ECG shows ST elevations in leads II, III, and aVF.

Which of the following represents the immediate changes taking place? (Note: LVEDV is left ventricular end diastolic volume, EF is ejection fraction, and PCWP is pulmonary capillary wedge pressure.)

|     | Blood Pressure | LVEDV     | EF        | PCWP      |
|-----|----------------|-----------|-----------|-----------|
| (A) | Increased      | Increased | Increased | Increased |
| (B) | Decreased      | Increased | Decreased | Increased |
| (C) | Decreased      | Increased | Increased | Increased |
| (D) | Decreased      | Increased | Decreased | Decreased |
| (E) | Decreased      | Decreased | Decreased | Decreased |

**The answer is C: Decreased blood pressure, increased LVEDV, increased EF, increased PCWP.** This patient is presenting with an inferior myocardial infarction (ST elevation in leads II, III, and aVF). In addition to this diagnosis, she is suffering from acute mitral regurgitation as a consequence



of papillary muscle rupture. This is one of the potential complications of myocardial infarctions and should be recognized by the physical examination finding of the classic murmur of mitral regurgitation. She has a normal blood pressure at this time, so she is compensating but is at risk for quickly decompensating.

As an acute response, the left ventricular ejection fraction will increase. Since fluid moves from high-pressure to low-pressure areas, the loss of chamber separation between the left ventricle and atrium by the mitral valve allows blood to be ejected from the left ventricle both into the aorta and into the low-pressure left atrium. In addition to this mechanism, the left ventricle will immediately see an increase in preload due to more blood returning to the ventricle that was ejected backward, and this will increase cardiac output by the Frank-Starling mechanism. Both of these mechanisms contribute to an increased ejection fraction. PCWP (equivalent to left atrial pressure) will increase due to backward flow of blood into the left atrium, and each time the ventricle relaxes during diastole there will be an increased volume of blood returning from the proximal circulation (increased LVEDV).

50

A 49-year-old man presents to clinic with diarrhea and periodic flushing. He reports that these symptoms have been present for several weeks, but he has been unable to seek medical attention until now. The diarrhea is profuse and watery, and he has had limited success with over-the-counter antidiarrheal medications. He denies any other medical problems, and has had no recent exposure to sick contacts. During the interview, the patient begins to flush in his face and neck. On examination, he has scattered wheezes throughout his lung fields as well as a systolic blowing murmur heard along the left sternal border.

If this disease process continues, the patient would develop deficiency of which of the following vitamins?

- (A) Niacin
- (B) Thiamine
- (C) Pyridoxine
- (D) Cobalamin

**The answer is A: Niacin.** This is a mechanistic question that is typical of the USMLE Step 1 examination, which tests primarily pathophysiology. Questions like these are rare on the shelf examination but do show up occasionally. The patient in this vignette presents with the classic features of carcinoid syndrome, which is caused by a neuroendocrine tumor that typically arises in the GI tract or bronchi. These tumors can secrete a variety of prostaglandins and amines (especially serotonin), which are responsible for the vasomotor symptoms. If the patient has a GI tumor, serotonin and any other secreted

products will be degraded by the liver before entering the systemic circulation. Therefore, symptoms usually develop after the tumor has metastasized to the liver. The most common symptoms are a result of the vasoactive secretory products and include periodic flushing of the face, neck, and chest, diarrhea, and bronchospasm. The diagnosis can be made by measuring elevated levels of 5-hydroxyindoleacetic acid (5-HIAA) in the urine, which is a serotonin metabolite. After the diagnosis is confirmed, the primary tumor should be localized and removed.

This patient also has evidence of carcinoid heart disease, which is caused by fibrous tissue deposition on the valvular surfaces of the right heart. Since the secreted products are degraded in the lungs, they do not typically affect the left heart. Murmurs of tricuspid and pulmonic regurgitation are common in carcinoid heart disease.

Serotonin is produced from the precursor amino acid tryptophan, which is also used to synthesize niacin (vitamin B<sub>3</sub>). Patients with carcinoid syndrome secrete high levels of serotonin and therefore deplete their stores of tryptophan. This can lead to niacin deficiency, which manifests as pellagra: Diarrhea, Dermatitis, and Dementia (mnemonic: B<sub>3</sub> deficiency → 3 D's). All of the other answer choices do not require tryptophan for synthesis. **(B)** Thiamine (vitamin B<sub>1</sub>) deficiency leads to beriberi and Wernicke–Korsakoff syndrome. This can be a result of malnutrition, so give alcoholics thiamine before administering glucose, as this can precipitate Wernicke encephalopathy. **(C)** Pyridoxine (vitamin B<sub>6</sub>) deficiency can cause sideroblastic anemia and peripheral neuropathy. This is a common side effect of isoniazid therapy and therefore pyridoxine should be supplemented during treatment. **(D)** Cobalamin (vitamin B<sub>12</sub>) deficiency leads to macrocytic anemia and subacute combined degeneration of the spinal cord (loss of proprioception and light touch due to damage of the dorsal columns).

51

A 20-year-old woman presents to the clinic with fever and arthritis. She reports that she developed these symptoms over the past few days, and the pain seems to be jumping from one joint to the next. There is no significant medical or family history, and she does not smoke or use illicit drugs. She reports that she had a throat infection 3 weeks ago, but she denies any recent exposure to sick contacts or recent sexual activity. The patient has a temperature of 38.6°C, blood pressure of 124/78 mmHg, heart rate of 88 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 100% on room air. On examination, she has a 2/6 blowing systolic murmur at the apex. There is erythema and swelling of her knees as well as her left elbow and wrist, and there are no skin or nail findings. Her white blood cell count is 15,000/mm<sup>3</sup> and the erythrocyte sedimentation rate is 45 mm/h. Antistreptolysin O titers are positive; blood cultures are drawn and are negative.

Which of the following is the most likely diagnosis?

- (A) Rheumatoid arthritis
- (B) Gonococcal arthritis
- (C) Rheumatic fever
- (D) Infective endocarditis

**The answer is C: Rheumatic fever.** One complication of untreated group A Streptococcal infection is rheumatic fever, which is an autoimmune disease that usually occurs 2 to 4 weeks after pharyngitis. It is usually seen in adolescents and is rare in adults. Diagnosis is made using the modified Jones criteria: evidence of strep infection plus two major criteria or one major criterion and two minor criteria. Major criteria include migratory polyarthritis, carditis, erythema marginatum (ring-like macular rash), Sydenham chorea, and subcutaneous nodules. Minor criteria include fever, arthralgia (painful joints without swelling), leukocytosis, elevated ESR or CRP, AV block on ECG, and previous rheumatic heart disease. This patient has two major criteria (polyarthritis and carditis) and three minor criteria (fever, leukocytosis, and elevated ESR), making the diagnosis of rheumatic fever likely. The murmur of mitral regurgitation in this patient is likely a result of valvulitis (meeting the criterion of carditis), since rheumatic fever can cause inflammation of any heart structure from the pericardium to the endocardium. Patients should be treated with antibiotics (penicillin) and aspirin if carditis is present.

(A) Rheumatoid arthritis may present with fever and symmetric polyarthritis; however, the temporal relation to pharyngitis should make the reader suspect rheumatic fever instead. (B) Gonococcal arthritis is a good diagnosis to consider in young sexually active patients presenting with fever, polyarthritis, and skin lesions (usually pustules). When this diagnosis is considered, cultures should be drawn from multiple sites (cervix, anus, synovium, etc.) to increase the diagnostic sensitivity; however, this patient is not sexually active and does not have any skin findings. (D) Infective endocarditis is diagnosed using the modified Duke criteria, which she does not meet. She has a new regurgitant murmur on examination; however, this can also occur in rheumatic fever from valvulitis.

52

A 38-year-old immigrant woman comes to the Emergency Department with right-sided weakness and slurring of her speech. Initial imaging and studies are obtained, and she is found to have suffered an ischemic stroke and is treated appropriately. When you go to examine her, she has an irregularly irregular pulse, and on cardiac examination she has an early diastolic high-pitched opening snap at the apex followed by a low-pitched diastolic rumbling murmur. Upon further discussion with the family, they indicate that she does not have any chronic medical problems and has not been to the doctor since she was

a baby. She had frequent throat infections as a child, but these always resolved without treatment. She takes no medications and does not smoke or drink alcohol.

The mechanism by which this condition developed is most similar to which of the following other conditions?

- (A) Infective endocarditis
- (B) Cystic fibrosis
- (C) Graves disease
- (D) Sarcoidosis
- (E) Guillain–Barré syndrome

**The answer is E: Guillain–Barré syndrome.** This is a difficult question that assumes a strong understanding of mitral stenosis, including the mechanism, diagnosis, and potential complications. This woman suffered a stroke, which is rare in her age group. A careful reading of the vignette shows that the patient had mitral stenosis and atrial fibrillation, both of which increase the propensity for a clot to form in the left atrium and embolize to the cerebral circulation to cause an ischemic stroke. The patient's history, obtained from her family, raises the suspicion for rheumatic heart disease as the cause of the patient's mitral stenosis. This is a common cause of mitral stenosis in developing countries and usually becomes symptomatic in the 30s. It is caused by *Streptococcus pyogenes* (Group A  $\beta$ -hemolytic strep). This is a reason why strep throat is important to diagnose and treat with antibiotics. Rheumatic heart disease is usually caused by repetitive strep infections, which was seen in this patient. The mechanism can be explained by the process of molecular mimicry, in which antibodies developed after exposure to an infectious agent cross-react with self antigens. One of these self antigens is present on the mitral valve, causing an autoimmune reaction which leads to scarring with subsequent repair and fibrosis, ultimately resulting in stenosis of the mitral valve. (E) Guillain–Barré syndrome is similarly a result of autoantibodies developed after exposure to an infectious agent (Campylobacter, Mycoplasma, viruses such as CMV and HIV, etc.) via the same mechanism of molecular mimicry. It results in an ascending paralysis due to demyelination of peripheral nerves.

(A) Infective endocarditis may affect the mitral valve, but damage of the valve commonly leads to a regurgitant murmur (rather than stenosis). The mechanism is by direct infection of the valve and not by an autoimmune process. (B) Cystic fibrosis is an autosomal recessive disease caused by a mutation in the CFTR gene encoding a chloride channel. (C) Graves disease is the result of autoantibodies against the TSH receptor, causing unregulated stimulation and secretion of thyroid hormone. There is no preceding infectious agent, and the autoantibodies are activating (not destructive). (D) Sarcoidosis is a granulomatous autoimmune disease but is not preceded by an infectious agent causing molecular mimicry.

53

A 42-year-old woman is brought to the hospital after losing consciousness. She was at an outdoor graduation ceremony when her daughter's name was called and she stood up with excitement. After she stood up, she felt lightheaded, nauseous, and started to develop tunnel vision. She tried to sit down but forgets what happened at this point. She awoke seconds later and was alert. She has a history of diabetes and GERD and takes metformin and omeprazole. There is no family history of heart disease or seizures. She is currently comfortable with no abnormalities on physical examination. Her blood pressure is normal and it does not change after going from a seated to a standing position.

Which of the following is the most likely diagnosis?

- (A) Arrhythmia
- (B) Orthostatic hypotension
- (C) Seizure
- (D) Vasovagal syncope

**The answer is D: Vasovagal syncope.** Syncope is defined as loss of consciousness that results from cerebral hypoperfusion. The most common cause of syncope is neurocardiogenic (vasovagal) syncope, which is caused by a sudden surge of sympathetic activity that transiently increases the contractility of the left ventricle. Mechanoreceptors in the left ventricle sense this increased contractility and cause an excessive vagal response, which lowers heart rate and contractility. This transiently drops the blood pressure and causes syncope. These patients typically have symptoms of lightheadedness, nausea, and narrowing vision prior to losing consciousness and can usually brace their fall somewhat. Diagnosis can be made with the tilt table test.

(A) Cardiovascular causes of syncope include arrhythmias, mechanical heart disease (e.g., aortic stenosis and hypertrophic cardiomyopathy), pulmonary embolism, aortic dissection, and cardiac tamponade. Patients with sudden onset syncope and trauma to the face (indicating an inability to brace the fall) should increase the reader's suspicion for a cardiac etiology. (B) Orthostatic hypotension usually occurs in the presence of hypovolemia, dysautonomia, and/or certain medications (e.g., diuretics and  $\beta$ -blockers). Diagnosis can be made if systolic blood pressure decreases by  $\geq 20$  mmHg or diastolic blood pressure decreases by  $\geq 10$  mmHg when going from a sitting to a standing position, which was not seen in this patient. (C) Seizures technically do not meet the definition of syncope, since they are not caused by a disruption in cerebral blood flow. History that would indicate a seizure include a preceding aura, tonic-clonic movements during the episode, and a postictal state (confusion with gradual improvement in neurologic function).

54

A 52-year-old woman presents with fatigue, peripheral edema, and periorbital purpura. She states that the symptoms of fatigue and

peripheral edema have developed gradually over the past few months, but the periorbital skin changes occurred abruptly after sneezing. She also experiences dyspnea after moderate exertion, which is abnormal for her. Her vitals are within normal limits. Her jugular veins are distended, and there are third and fourth heart sounds. Her lungs are clear bilaterally and she has pitting edema around the ankles. A urinalysis reveals significant proteinuria, and an ECG shows low voltages throughout all the leads. The patient is admitted and a cardiac biopsy is performed. The tissue is stained with Congo red and shows apple-red birefringence under polarized light.

Which of the following is the correct diagnosis?

- (A) Amyloid cardiomyopathy
- (B) Hypertrophic cardiomyopathy
- (C) Rheumatoid arthritis
- (D) Hemochromatosis
- (E) Temporal (giant cell) arteritis

**The answer is A: Amyloid cardiomyopathy.** The stain showing apple-red birefringence should lead the reader to suspect amyloidosis as the cause of this patient's restrictive cardiomyopathy. There are several types of amyloidosis that can cause restrictive cardiomyopathy, and in this case the patient most likely has the AL form that is a primary disease process resulting from a plasma cell dyscrasia. In this form of the disease, light chain proteins are deposited in tissues throughout the body, and the heart is commonly affected with a poor prognosis. The periorbital purpura is fairly specific for the AL form. Inherited amyloidosis and senile amyloidosis fall into a separate category called ATTR amyloidosis, which results from an autosomal dominant mutation in the gene encoding transthyretin. The AA form occurs as a secondary disease process that results from deposition of serum amyloid A protein. It may occur with chronic inflammatory conditions such as rheumatoid arthritis or inflammatory bowel disease; however, this form does not commonly lead to heart disease. Treatment in AL amyloidosis is twofold: chemotherapy for the underlying process, and treatment of the heart failure with typical agents (although ACE inhibitors and  $\beta$ -blockers are typically not tolerated in amyloid cardiomyopathy).

(B) Hypertrophic cardiomyopathy would show an S4 but not an S3 on examination, and would show left ventricular hypertrophy on ECG (not low voltages as is seen with infiltrative processes like amyloidosis). (C) Rheumatoid arthritis can cause inflammation of heart structures (pericarditis, endocarditis, etc.), but she has no other suggestive symptoms. It may cause AA amyloidosis; however, this form does not typically affect the heart. (D) Hemochromatosis can cause a restrictive cardiomyopathy but this typically presents in men with skin darkening, arthritis, diabetes, and liver disease. (E) Temporal arteritis is a vasculitis that presents in older patients with fever, headache, jaw claudication,

and tenderness over the temporal arteries. It is often associated with polymyalgia rheumatica. Biopsy of the temporal artery shows intimal thickening and granulomatous inflammation.

55

A 46-year-old man with a history of familial hypercholesterolemia is admitted to the hospital for chest pain. He is found to have a massive myocardial infarction and undergoes PCI. The following day, the patient becomes hypotensive, and on examination he has distant heart sounds.

Which of the following should be avoided in this patient?

- (A) IV normal saline
- (B) Inotropic agents
- (C) Immediate surgery
- (D) Immediate pericardiocentesis

**The answer is D: Immediate pericardiocentesis.** This patient is presenting with a complication of a massive MI, which is ventricular free wall rupture leading to cardiac tamponade. This usually occurs within the first few days after an MI and presents with Beck's triad of cardiac tamponade: hypotension, distended neck veins, and muffled/distant heart sounds. Free wall rupture leading to tamponade may also present with pulseless electrical activity. As blood accumulates in the pericardial sac, it exerts pressure on the heart and causes an equalization of pressure within the four chambers. During inspiration, blood is drawn into the right ventricle due to the negative intrathoracic pressure, and the interventricular septum deviates into the left ventricle and reduces left ventricular preload, and therefore the cardiac output. A paradoxical elevation in jugular venous pressure during inspiration may be seen in cardiac tamponade, but is also seen in other conditions including constrictive pericarditis (Kussmaul sign). This is a life-threatening situation, and immediate surgery is often necessary.

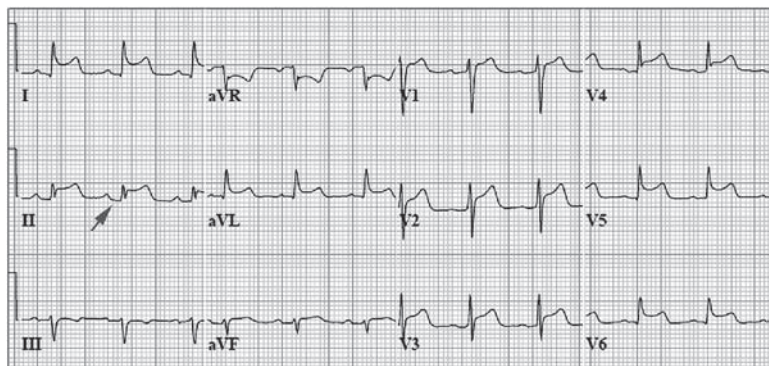
(D) The patient is hemodynamically unstable, and all the choices except pericardiocentesis are appropriate in this setting. (A) IV fluids can increase preload for adequate filling of the ventricles, which can help to offset the decreased cardiac output. (B) Inotropic agents may be necessary to support the blood pressure since he is hypotensive. Immediate pericardiocentesis is not a good option in this case, since it will not correct the underlying problem (a hole in the ventricular wall); drawing off a small amount of fluid in the setting of pulseless electrical activity may be appropriate, but in this scenario the patient should undergo immediate surgery to correct the ventricular defect.

56

A 32-year-old woman presents to the hospital with chest pain. She states that the pain is sharp, worse with deep inspiration, and is somewhat



relieved by leaning forward. She is febrile and a friction rub is heard on examination. An ECG is shown below (Figure 1-13).



**Figure 1-13**

The patient is offered treatment but refuses all medications. Which of the following is the most common complication if this disease remains untreated?

- (A) Cardiac tamponade
- (B) Recurrent pericarditis
- (C) Constrictive pericarditis
- (D) Ventricular free wall rupture
- (E) Valvular insufficiency

**The answer is B: Recurrent pericarditis.** The chest pain and ECG are typical of acute pericarditis, which commonly presents with fever, pleuritic chest pain, new onset pericardial effusion, and diffuse concave ST elevations on ECG. Most cases have an infectious etiology, including Coxsackie viruses, HIV, influenza, *S. aureus*, *S. pneumoniae*, tuberculosis, and various fungi. Other important causes include cancer, autoimmune diseases, post-MI or cardiac surgery, radiation therapy, and uremia. All patients should be treated with NSAIDs and colchicine to improve symptoms and prevent complications. Patients who are not treated are much more likely to develop recurrent pericarditis, which is defined as a recurrence of symptoms after the inciting event (e.g., virus) has passed. (A) Pericardial effusions commonly accompany acute pericarditis; however, cardiac tamponade is a rare complication. (C) Constrictive pericarditis is a possible outcome of any cause of acute pericarditis; however, it is not the most common complication. (D) Free wall rupture is a complication of acute myocardial infarction. (E) Pericarditis affects the pericardium although the myocardium is sometimes affected as well. However, the rate of valve involvement and complications is low.



57

A young man with Marfan syndrome is brought in by paramedics with sharp chest pain that radiates to his back. Shortly after the pain started, he developed left-sided weakness. The chest pain progressed and an ambulance was called. The initial blood pressure recorded by paramedics on the right arm was 78/54 mmHg, but a reading from the left arm shows 114/74 mmHg. An ECG is performed and shows ST elevations in the anterolateral leads. There is widening of the mediastinum on chest x-ray.

Which of the following is the most likely underlying diagnosis?

- (A) Myocardial infarction
- (B) Aortic dissection
- (C) Stroke
- (D) Acute aortic regurgitation

**The answer is B: Aortic dissection.** The most important risk factor for aortic dissection in the general population is hypertension; however, there is a high incidence in patients with connective tissue disease (e.g., Marfan and Ehlers–Danlos syndromes). Sharp chest pain radiating to the back is the first clue to this diagnosis. Other symptoms may occur based on which arteries are occluded by the dissected flap. This patient has a dissection of the ascending aorta, since he has symptoms/signs involving the left coronary artery (ST elevations in the anterolateral distribution) and brachiocephalic artery (affecting the right coronary artery leading to symptoms of stroke and the right subclavian artery leading to a decrease in systolic blood pressure >20 mmHg in the right arm compared to the left). Other potential manifestations not seen in this patient are cardiac tamponade and Horner syndrome (from compression of the superior cervical ganglion). Dissections involving the proximal aorta require immediate surgical intervention.

(A, C, D) All of these diagnoses are a result of the patient's aortic dissection, but are not the underlying (primary) diagnosis. ACS may occur during an aortic dissection as a result of involvement of one or more coronary arteries, and stroke can occur with involvement of the carotid arteries. Aortic regurgitation is common in patients with Marfan syndrome, and this can also occur as a result of a dissection in the ascending aorta. In either situation, it is not the primary diagnosis.

58

A 62-year-old Caucasian man with a history of diabetes and a myocardial infarction 2 years ago is hospitalized for acute decompensated heart failure. He is diuresed with improvement in symptoms and is discharged on appropriate medications. He is seen in clinic 4 months later with complaints of worsening symptoms over the last month. Previously he became mildly short of breath after significant exertion, but he now reports severe shortness of breath after walking only 50 m. He

is asymptomatic only at rest. His current medications include aspirin, captopril, carvedilol, furosemide, atorvastatin, omega-3 fatty acids, and pantoprazole. An ECG performed in the office shows Q waves in leads V3 and V4, with a normal QRS duration. An echocardiogram performed 1 week ago showed an ejection fraction of 35%.

The patient has been encouraged to quit smoking and drinking alcohol, and to eat a low-sodium diet. What additional therapy is recommended at this time?

- (A) Losartan
- (B) Spironolactone
- (C) Cardiac resynchronization therapy
- (D) Hydralazine and isosorbide dinitrate
- (E) Both B and C
- (F) None of the above

**The answer is B: Spironolactone.** This question tests the reader's understanding of chronic heart failure treatment. The patient displays New York Heart Association (NYHA) class III symptoms (no symptoms at rest, but symptoms with minimal exertion), and therefore needs an escalation in his treatment. He is on an appropriate initial regimen, which includes a loop diuretic, an ACE inhibitor, and a  $\beta$ -blocker. Angiotensin receptor blockers (ARBs) are appropriate alternatives to ACE inhibitors, but should not be used in conjunction with ACE inhibitors. The three  $\beta$ -blockers shown to have a survival benefit in heart failure are carvedilol, metoprolol, and bisoprolol, so one of these agents is usually used. This patient is symptomatic and needs the next step in therapy, which is an aldosterone antagonist (e.g., spironolactone). These agents reduce mortality in patients with NYHA class III/IV with a reduced ejection fraction ( $\leq 35\%$ ), or in patients with heart failure that have suffered a previous myocardial infarction. Notable side effects of spironolactone include hyperkalemia, gynecomastia, and agranulocytosis. If the patient is still symptomatic, digoxin may be prescribed although there is no mortality benefit with this agent. The patient should also consider an ICD given his history of myocardial infarction and reduced ejection fraction. ICDs have been shown to reduce mortality, both for primary prevention and for secondary prevention of fatal arrhythmias.

(A) The patient is already on an ACE inhibitor, and there is no benefit to adding an angiotensin receptor blocker. (C) Cardiac resynchronization therapy (CRT) may be considered in heart failure patients with dyssynchrony between the left and right ventricles, and therefore criteria for CRT includes a QRS duration  $>120$  ms. This patient does not meet criteria. (D) Hydralazine and nitrates are used as alternatives to ACE inhibitors and ARBs if the patient cannot tolerate one of these agents. Hydralazine and nitrates are especially beneficial for African Americans, but this patient is Caucasian.

59

A 42-year-old man presents to the hospital with worsening leg swelling and exertional dyspnea. He denies any recent illness, fevers, weight loss, cough, chest pain, or abdominal pain. His medical history is significant for Hodgkin lymphoma at the age of 20, and he has been in remission after treatment with chemotherapy and radiation. He does not smoke or drink alcohol, and he denies any recent travel or new environmental exposures. His vitals are normal, and there is no scleral icterus or cervical lymphadenopathy. The jugular venous pressure is elevated and increases further during inspiration. Heart sounds are distant with no S3, and the lungs are clear bilaterally. There is hepatomegaly and pitting edema of the lower extremities. A chest x-ray shows a normal heart border without any pulmonary infiltrates. An echocardiogram is performed that shows normal wall thickness with no significant pericardial effusion.

Which of the following is the most likely diagnosis?

- (A) Pulmonary hypertension
- (B) Dilated cardiomyopathy
- (C) Restrictive cardiomyopathy
- (D) Constrictive pericarditis

**The answer is D: Constrictive pericarditis.** Patients with previous radiation therapy to the chest are at risk for constrictive pericarditis, which is a result of thickening and decreased compliance of the pericardium. Any cause of acute pericarditis can progress to constrictive pericarditis. These patients present with symptoms of right-sided heart failure and Kussmaul sign, which is a paradoxical increase in jugular venous pressure during inspiration. (C) Kussmaul sign can also be seen in restrictive cardiomyopathy; however, the echocardiogram did not show an increase in myocardial wall thickness and therefore the more likely diagnosis is constrictive pericarditis. (A) Pulmonary hypertension may cause right-sided heart failure but would not present with Kussmaul sign. (B) There are many causes of dilated cardiomyopathy, including radiation exposure; however, Kussmaul sign should lead the reader to think of constrictive pericarditis. In addition, the chest x-ray did not show an enlarged heart.

60

A 73-year-old man with severe aortic stenosis presents to the hospital after passing a moderate amount of blood per rectum. Over the past few years, he has noticed easy bruising and frequent nose bleeds. He has no history of a bleeding disorder, and has no family history of such conditions. He does not take any medications. His vitals are normal, and the examination is unremarkable except for the murmur of aortic stenosis. Laboratory values are drawn and show a hemoglobin level of 11 g/dL and a normal prothrombin time (PT) and partial thromboplastin time (PTT). Factor VIII levels are decreased.

What is the most likely explanation for the episodes of bleeding in this patient?

- (A) Clotting factor deficiency
- (B) Platelet deficiency
- (C) Defect in platelet adhesion
- (D) Inhibition of antithrombin III
- (E) Vitamin K deficiency

**The answer is C: Defect in platelet adhesion.** Patients with severe aortic stenosis are at risk for von Willebrand disease (vWD). This is caused by a qualitative deficiency of von Willebrand factor (vWF), which functions in platelet adhesion during coagulation. The name of this condition is Heyde syndrome, and the most dangerous complication is bleeding in the GI tract from angiodysplasias. In severe aortic stenosis, the shear forces on the blood passing through the stenotic valve cause proteolysis of vWF, making it ineffective. vWF also functions to carry factor VIII in the plasma, which is degraded rapidly if not bound to vWF. Therefore, patients with vWD will present with bleeding from skin and mucosal surfaces and low levels of factor VIII; PTT may or may not be prolonged, and PT will be normal. Diagnosis can be made by first measuring vWF antigen (quantitative assay), vWF activity (ristocetin cofactor, a qualitative assay), and factor VIII levels. Confirmation can be made with more specialized tests, such as vWF multimer analysis.

(A) Although these patients will have factor VIII deficiency, PTT is not always prolonged and the cause of their prolonged bleeding is due to platelet adhesion, not clotting factor deficiency. (B) Some patients may have mildly decreased platelet levels, but the abnormal bleeding is due to problems in platelet adhesion (not platelet count). (D) Inhibition of antithrombin III is the mechanism of heparin. (E) There is nothing to suggest malnutrition in this patient, and the patient is not taking warfarin, which inhibits vitamin K epoxide reductase and decreases functional vitamin K, which is responsible for activating clotting factors II, VII, IX, and X.

## Pulmonology

1

A 68-year-old woman is hospitalized for an acute exacerbation of chronic obstructive pulmonary disease (COPD). She responds well to treatment and is discharged. At her follow-up appointment, she states that she has been compliant with treatment but has had 2 acute exacerbations in the last 9 months. In addition to COPD, her medical history is significant for hypertension, hyperlipidemia, and atrial fibrillation. She takes hydrochlorothiazide, simvastatin, diltiazem, and salmeterol. She also takes inhaled albuterol and ipratropium as needed. She does not smoke, is up to date with the appropriate vaccinations, and is undergoing pulmonary rehabilitation. Her vitals are taken: blood pressure 132/86 mmHg, heart rate 87 beats per minute, respiratory rate 16 breaths per minute, and oxygen saturation 94% on room air.

Which of the following is the most appropriate next step in management?

- (A) Add theophylline
- (B) Add inhaled fluticasone
- (C) Add oral prednisone
- (D) Start home oxygen therapy
- (E) No change

**The answer is B: Add inhaled fluticasone.** This patient's COPD is progressively worsening and she suffered another acute exacerbation, which makes it necessary to step up her treatment to the next level. Treatment of COPD progresses in a stepwise fashion based on symptoms, number of exacerbations, and GOLD staging criteria, which relies on forced expiratory volume in 1 second (FEV<sub>1</sub>) for staging. For the shelf examination, the most important task is to recognize when a patient requires a step-up in therapy and then to know what the next step in therapy is. The first step in all of these patients is to decrease risk factors: smoking cessation and vaccinations to prevent lung infections (pneumococcal vaccine and annual influenza vaccine). Pulmonary



## BOX 2-1 Step-Up Therapy for COPD

- Short-acting bronchodilators as needed:  $\beta_2$  agonists (e.g., albuterol), anticholinergics (e.g., ipratropium), or a combination of both
- Long-acting bronchodilators: either a long-acting  $\beta$  agonist (LABA; e.g., salmeterol) or a long-acting muscarinic agent (LAMA; e.g., tiotropium)
- Inhaled corticosteroids (e.g., fluticasone); should not be used alone without a long-acting bronchodilator (increased risk of pneumonia); a second long-acting agent may also be added (triple inhaler therapy: inhaled corticosteroid + LABA + LAMA)
- Home  $O_2$  if  $S_aO_2 \leq 88\%$  or  $P_aO_2 \leq 55$  mmHg; if refractory disease, theophylline or experimental therapies

rehabilitation is another supplemental therapy that is useful in patients with at least moderate symptoms. The treatment steps in pharmacologic therapy are summarized in *Box 2-1* in a stepwise fashion; when a patient is experiencing worsening of symptoms or acute exacerbations, the next step should be added to the current regimen.

Other complicated treatments for advanced disease, such as lung volume reduction surgery, are not typically tested on the shelf examination. This patient's regimen includes short-acting bronchodilators and a LABA, and therefore the next step in management is an inhaled corticosteroid.

(A) Theophylline blocks phosphodiesterase and increases intracellular cAMP, leading to increased catecholamine release. It is not a first-line therapy, but it may be used in severe COPD for refractory disease. As a sympathomimetic, it can exacerbate tachyarrhythmias and therefore is not a good option in this patient with atrial fibrillation. (C) Oral corticosteroids are used for acute exacerbations but not in chronic disease due to the negative side-effect profile as well as an increase in mortality. (D) This patient does not meet criteria for home oxygen therapy at this time (criteria explained later). (E) The patient has worsening symptoms and the next step in therapy is warranted.



2

A 33-year-old alcoholic man is hospitalized for fever, chills, and cough productive of currant jelly sputum. Blood and sputum cultures are drawn, and a chest x-ray is consistent with lobar pneumonia. Urine toxicology screen and a serum ethanol level are negative. After being admitted and started on empiric antibiotics, he continues to decompensate and becomes more hypoxemic based on pulse oximetry.

Which of the following choices best represents the pathophysiologic parameters seen in this patient? (Note: A–a gradient is Alveolar–arterial gradient;  $\text{FiO}_2$  is the fraction of inspired oxygen.)

|     | $\text{PaO}_2$ | $\text{PaCO}_2$ | A–a Gradient | Response to Increased $\text{FiO}_2$ |
|-----|----------------|-----------------|--------------|--------------------------------------|
| (A) | Low            | Normal          | Increased    | Improvement                          |
| (B) | Low            | Normal          | Increased    | No change                            |
| (C) | Low            | Low             | Normal       | No change                            |
| (D) | Low            | High            | Normal       | Improvement                          |

**The answer is B: Low  $\text{PaO}_2$ , normal  $\text{PaCO}_2$ , increased A–a gradient, and no change in response to increased  $\text{FiO}_2$ .** This question assumes a background knowledge of the physiology of gas exchange and how to differentiate between hypoxemic and hypercapnic respiratory failure. Most cases of hypoxemia involve an elevation in the Alveolar–arterial (A–a) gradient, which is the product of the partial pressure of alveolar oxygen ( $\text{PAO}_2$ ) minus the partial pressure of arterial oxygen ( $\text{PaO}_2$ ). The A–a gradient normally increases with aging and is represented by the formula: “age/4 + 4.” (Although there is an equation for calculating the  $\text{PAO}_2$ , the concept is more important than the equation for the shelf examination.) There are many causes of hypoxemia, and it is best to use a systematic approach for this discussion.

The causes of respiratory failure can be broken up by whether there is hypoxemia with a low/normal  $\text{PaCO}_2$  (hypoxemic respiratory failure) or there is hypoxemia and an elevated  $\text{PaCO}_2$  (hypercapnic respiratory failure). Major causes of hypoxemic respiratory failure include ventilation/perfusion (V/Q) mismatch, right-to-left shunts, and diffusion impairment. V/Q mismatch is a disease process that causes an imbalance between blood flow and gas exchange, which decreases the efficiency of gas exchange and causes hypoxemia. This is really a gray zone in between two states: if taken to one end of the spectrum with a pure loss of perfusion (e.g., pulmonary embolism), this causes “dead space ventilation” (normal air flow but no blood flow). If taken to the other end of the spectrum with a pure loss of ventilation (e.g., atelectasis or pneumonia with consolidation), then this becomes a shunt. Shunts are simply the result of blood bypassing any area of gas exchange, carrying hypoxemic blood back into the circulation. Shunts can also be extrapulmonary (e.g., intracardiac shunts like an atrial septal defect). An example of diffusion impairment is interstitial lung disease with fibrosis that increases the distance that oxygen must traverse to get from the alveoli to the blood stream; processes that increase the rate of blood flow (exercise) or decrease the oxygen-carrying capacity (anemia) can exacerbate hypoxemia caused by diffusion impairment. Other causes besides the above three mechanisms include

poisoning (carbon monoxide, methemoglobinemia, and cyanide) and high altitudes (same fraction of inspired oxygen but lower atmospheric pressure).

Hypercapnic respiratory failure is caused by inadequate ventilation (respiratory rate  $\times$  tidal volume), and results from processes such as neuromuscular disease, oversedation, COPD, and obesity hypoventilation syndrome. In hypoxemic respiratory failure, the patient attempts to compensate for the hypoxemia by increasing ventilation, which results in a normal or low PaCO<sub>2</sub>.

This patient has hypoxemic respiratory failure from pneumonia, and there are no reasons for hypoventilation (no sedation and a negative drug screen). In a process like a lobar pneumonia, where alveoli are completely filled with pus, shunting will predominate over V/Q mismatch and therefore the hypoxemia will not be corrected with increased oxygen administration. Positive end-expiratory pressure (PEEP) might help to open some of the alveoli in areas of consolidation, converting a shunt to a V/Q mismatch, but this question asks about the response to FiO<sub>2</sub> alone.

**3** A 62-year-old woman presents to the hospital with shortness of breath. She has a history of HIV infection and was recently hospitalized for PCP pneumonia and was discharged 3 days ago in stable condition on oral antibiotics. After discharge, she started to experience a headache and subsequently developed worsening shortness of breath. The rest of her medical history is significant for hypertension, diabetes, peripheral arterial disease, hypothyroidism, and gastroesophageal reflux disease (GERD). Her regular medications include aspirin, amlodipine, hydrochlorothiazide, metformin, levothyroxine, and pantoprazole. She has not been compliant with her antiretrovirals. Her allergies include trimethoprim-sulfamethoxazole and penicillin. She drinks alcohol moderately and has a 30 pack-year smoking history. On examination, she has a temperature of 37.6°C, blood pressure of 158/96 mmHg, heart rate of 86 beats per minute, and respiratory rate of 26 breaths per minute. There are no murmurs or jugular venous distention, and there are no wheezes or rales on pulmonary examination. There is blue discoloration of her digits and lips. An arterial blood gas shows a normal PaO<sub>2</sub>, although the blood has a brownish discoloration.

Which of the following is the most likely diagnosis?

- (A) Chronic obstructive pulmonary disease
- (B) Bronchiectasis
- (C) Pneumonia
- (D) Acute respiratory distress syndrome
- (E) Congestive heart failure
- (F) Carbon monoxide poisoning
- (G) Methemoglobinemia



**The answer is G: Methemoglobinemia.** The differential of dyspnea is broad, but it can be narrowed based on the history and physical examination (even in a complicated patient like this one!). The two broad categories that can be considered first are pulmonary and cardiovascular disease. Pulmonary disease may be broken down into airway disease (e.g., bronchitis, asthma, bronchiectasis, tumor), parenchymal disease (e.g., interstitial lung disease, pulmonary edema), or pleural disease (e.g., pleural effusion). Important cardiovascular diseases that cause dyspnea include left heart failure, pulmonary hypertension, pulmonary embolism, and vasculitides affecting the pulmonary vasculature.

In addition to these two categories, there are neuromuscular causes (e.g., myasthenic crisis), metabolic causes (e.g., metabolic acidosis), psychological causes (e.g., panic disorder), and causes relating to the oxygen-carrying capacity of the blood. The diagnosis in this case relates to this last category. Methemoglobinemia may be congenital or acquired, and certain medications such as dapsone and nitric oxide can cause methemoglobinemia. The pathophysiology involves oxidation of iron to the ferric state ( $\text{Fe}^{3+}$ ), which cannot bind oxygen but causes the other heme groups in hemoglobin to bind oxygen more tightly, shifting the hemoglobin dissociation curve to the left. The result is an inability of the circulating hemoglobin to provide oxygen to tissues.  $\text{PaO}_2$  will be normal and the pulse oximetry will typically be in the 85% to 89% range. The blood is sometimes described as “chocolate blood” due to its dark red or brown appearance. Treatment is with methylene blue, an agent that reduces  $\text{Fe}^{3+}$  back to  $\text{Fe}^{2+}$ . This patient likely has methemoglobinemia secondary to dapsone, since dapsone is an alternative to trimethoprim-sulfamethoxazole for the treatment of PCP pneumonia.

(A, B, C, D, E, H) The rest of these conditions, except for carbon monoxide poisoning, would have a depressed  $\text{PaO}_2$ . (F) Carbon monoxide poisoning may present with headache and cyanosis due to carbon monoxide displacing oxygen from heme and reducing the oxygen carrying capacity of the blood. Pulse oximetry and  $\text{PaO}_2$  will be normal in this condition.



A 19-year-old boy complains of difficulty breathing during exercise. He reports being in good physical shape, but occasionally experiences coughing and have to stop and catch his breath. This seems to occur more often in cold weather. The patient has no significant medical history other than seasonal allergies, and he takes no medication. He has some patchy dry skin over the elbows with some erythema and excoriations; otherwise the physical examination is normal. He is referred for spirometry, which is normal.

Which of the following is the most appropriate next step in management?

- (A) Albuterol challenge
- (B) Methacholine challenge
- (C) Chest x-ray
- (D) Allergen skin testing
- (E) Trial of albuterol

**The answer is B: Methacholine challenge.** Although the diagnosis of asthma is tested more often on the Pediatrics shelf examination, it may show up on the Medicine shelf examination and therefore a brief overview may be useful. Asthma is an intermittent obstructive lung disease that is classically described as airway hyper-responsiveness with variable airflow obstruction. It is a common condition, especially in those with other features of the atopic triad (seasonal allergies, eczema, and asthma). Symptoms are usually caused by common triggers such as infections, environmental exposures (smoke, allergens, etc.), medications ( $\beta$ -blockers, aspirin, NSAIDs), cold air, and exercise. Because symptoms of asthma may be intermittent, the physical examination is often normal. If spirometry is consistent with an obstructive pattern, then asthma can be differentiated from COPD by assessing the improvement in FEV<sub>1</sub> after bronchodilator administration (e.g., albuterol); if FEV<sub>1</sub> improves by at least 12%, then the diagnosis is more consistent with asthma. If spirometry is normal, as in this patient, a provocative test such as the methacholine challenge can be performed. Methacholine is a muscarinic agonist that will cause bronchoconstriction; asthmatics will be much more sensitive to lower doses of methacholine than the regular population and will develop an obstructive pattern on spirometry with a prolonged FEV<sub>1</sub>.

(A) This patient has normal findings on spirometry and therefore the administration of albuterol will not change the findings. (C) A chest x-ray would likely be normal in this patient. During an acute exacerbation, there may be hyperinflation of the lungs. (D) Allergen skin testing is not a bad idea, especially since the patient has a history of seasonal allergies and eczema, but it is not the best next step in management. (E) If the initial workup is negative, then the patient might be encouraged to measure peak expiratory flow or try a bronchodilator while symptomatic. Since he is undergoing spirometry already, a methacholine challenge should be attempted first to make the diagnosis.

**5** A 38-year-old woman presents to the hospital with fever, cough, and shortness of breath. On imaging, a lobar pneumonia is confirmed, but a lung mass is also noted. She is treated with antibiotics and at a later time the mass is biopsied via bronchoscopy. Eventually the patient is discharged to follow up as an outpatient. The biopsy report suggests a benign lesion, and the patient agrees to have the lesion followed with imaging. Several months later, the patient presents with difficulty breathing

for a few weeks. Her vitals are normal, but inspiratory and expiratory stridor is heard along with rhonchi on lung auscultation. There are no wheezes or rales. Examination of the oropharynx is unremarkable. Spirometry with flow-volume loops shows a plateau during inspiration and expiration, with decreased peak inspiratory and expiratory flow.

What is the most likely diagnosis?

- (A) Subglottic stenosis
- (B) Carcinoid tumor
- (C) Viral bronchiolitis
- (D) Postobstructive pneumonia

**The answer is A: Subglottic stenosis.** Auscultation of lung sounds helps to define the site of pathology within the airway anatomy. Rhonchi are low-pitched, sonorous sounds that typically indicate secretions in the upper airway. High-pitched sounds as a result of upper airway obstruction are termed stridor. Wheezes are high-pitched musical sounds caused by narrowing of bronchioles. Rales, also known as crackles, come in two types (wet and dry), and the pathology in both types involve the distal airway. Wet rales are caused by fluid accumulation within alveoli, which overwhelms the mechanism of surfactant to decrease surface tension and causes the alveoli to collapse and open back up during the end of inspiration; dry rales (velcro sound) typically involve the smaller airways leading into the alveoli and are usually due to interstitial processes such as pulmonary fibrosis.

This patient has stridor, which suggests that the problem involves the upper airway. In addition, the reduction in peak inspiratory and expiratory flow with plateaus seen on the flow-volume loops are indicative of a fixed obstruction. The only answer choice that fits with a fixed obstruction of the upper airway is subglottic stenosis, which can be congenital or acquired from trauma during procedures such as bronchoscopy. The rhonchi are likely a result of excess secretion build up below the obstruction. It is likely that the tumor is indeed benign and is not responsible for this patient's symptoms. (B, C) A carcinoid tumor and viral bronchiolitis would both produce wheezing, which is not heard in this patient. (D) Postobstructive pneumonia could occur in this patient given that she has a lung mass near the airway, however this would produce rales and not stridor.

6

A 27-year-old Asian man presents to the Emergency Department after coughing up a large amount of blood, which has never happened before. He has a history of oral and genital ulcerations that were diagnosed as herpes, but the lesions have never responded to antivirals. His family history is noncontributory, he does not smoke or use illicit drugs, and he has not traveled recently. He lives in an urban area and has never been imprisoned. On review of systems, he endorses some vision changes and occasional joint pain, but denies any recent illnesses, weight loss, night sweats, cough (prior to the hemoptysis), or hematuria. His examination

is significant for oral and genital ulcerations that are painful to palpation, and examination of the eyes shows ciliary flush with some floating debris in the anterior chamber. His laboratory values show a normal BUN and creatinine.

Which of the following is the most likely diagnosis?

- (A) Granulomatosis with polyangiitis
- (B) Behçet disease
- (C) Pulmonary embolism
- (D) Bronchiectasis
- (E) Lung cancer
- (F) Congestive heart failure
- (G) Tuberculosis
- (H) Coccidioidomycosis

**The answer is B: Behçet disease.** The point of this question is to test the reader's understanding of the differential diagnosis of hemoptysis. Anything that damages the pulmonary vasculature can present with hemoptysis. Important high yield causes that you should always consider are tuberculosis and lung cancer. Other pulmonary causes include bronchitis, bronchiectasis, and pneumonia. Infectious etiologies include lung abscesses, fungal infections such as coccidioidomycosis and aspergillomas, and any cause of pneumonia. Direct damage of the vasculature from a pulmonary embolism or vasculitis can cause massive hemoptysis. Cardiac disease causes vessel damage from elevated pressures within the pulmonary vasculature, and common causes include CHF and mitral stenosis. GI bleeding can sometimes be mistaken for hemoptysis (e.g., Mallory–Weiss tears in the gastroesophageal junction from severe retching).

Behçet disease is a vasculitis that can affect any vessel size and is more common in people from areas along the ancient Silk Road (highest incidence is in Turkey). Common manifestations include oral and genital ulcerations, uveitis, venous thrombosis, arterial aneurysm and hemorrhage (e.g., hemoptysis), skin changes, joint pain, and neurologic changes. The diagnosis is made based on clinical findings, and treatment is with colchicine or immunosuppressants. Even if the reader was unfamiliar with this diagnosis, they could have used the process of elimination to make a good guess.

(A) Granulomatosis with polyangiitis (Wegener) and Goodpasture syndrome both affect the kidneys and lungs, but this patient does not have renal involvement. (C, D) Bronchiectasis and pulmonary embolism are not suggested by the history; in bronchiectasis, look for a history of recurrent sinopulmonary disease (cystic fibrosis), and for pulmonary embolism look for thrombotic risk factors (recent travel, surgery, OCPs, etc.). (E) The patient is young with no smoking history and no symptoms of weight loss or night sweats; therefore lung cancer is unlikely. (F) There are no findings of CHF on examination (e.g., jugular venous distention, pedal edema). (G) Tuberculosis is suggested by sick exposures, travel to an endemic area, a history of imprisonment, and symptoms

of cough and night sweats. (H) This patient lives in an urban environment, and *Coccidioides immitis* is found in desert regions (Arizona and the central valley of California).

**7** An older man with a history of COPD complains of worsening dyspnea and exercise intolerance, even after smoking cessation and an evidence-based pharmacologic regimen. The physician discusses the possibility of adding theophylline to the patient's chronic regimen.

What potential adverse reaction should the patient be counseled about before starting this medication?

- (A) Bradycardia
- (B) Pulmonary fibrosis
- (C) Hypocalcemia
- (D) Seizures

**The answer is D: Seizures.** Theophylline is a methylxanthine drug that acts as a phosphodiesterase inhibitor and increases bronchodilation. It is not a first-line treatment for COPD or asthma, but it may be an adjunctive treatment in select patients for chronic COPD or asthma. This medication has a narrow therapeutic index and may cause arrhythmias, seizures, and persistent vomiting. It should be used with caution in patients with cardiac disease, hyperthyroidism, peptic ulcer disease, and a seizure disorder, since it can exacerbate these conditions. (A, C) Theophylline may cause tachycardia and hypercalcemia. (B) It does not cause pulmonary fibrosis.

**8** A 24-year-old woman with a history of asthma complains of worsening chest tightness and cough. She currently has an albuterol inhaler that she uses as needed, but says that it does not help very much. She has no other medical problems and takes no other medications. The physical examination is unremarkable.

Which of the following is the most appropriate next step in management?

- (A) Add an inhaled corticosteroid
- (B) Add an inhaled anticholinergic
- (C) Education about proper use of inhalers
- (D) Workup for a different diagnosis

**The answer is C: Education about proper use of inhalers.** Education is truly a cornerstone of asthma therapy. Patients should be educated about how to properly use their inhaler, how to monitor their pulmonary function (with peak expiratory flow), and how to recognize and avoid triggers. Proper education about inhalers includes shaking the medication before use, correct positioning, taking a slow deep breath while administering the medication, and

holding the medication within the lungs for at least 5 seconds before breathing out. In addition to the importance of technique, patients should also be educated about the timing of use. Patients that know that they will be experiencing a trigger should use the inhaler 10 minutes in advance (e.g., used before exercise). As a general rule, the correct answer on the shelf examination usually follows the principle that the least invasive maneuver should be attempted first, and therefore choices such as obtaining a further history and patient education are usually the right answers. **(A)** An inhaled corticosteroid is the next step in therapy for worsening symptoms, however an additional medication might be avoided in this patient if she begins to use her inhaler correctly. **(B)** An inhaled anticholinergic such as ipratropium can be used to improve delivery of the  $\beta_2$  agonist reliever medications and improve bronchodilation, but this is not the next step. **(D)** Medication compliance and proper technique should be addressed before assuming that the diagnosis of asthma is incorrect.



A 37-year-old Caucasian man presents with a several-month history of intermittent fevers, chills, chest tightness, and shortness of breath. The episodes typically occur on weekends and are most pronounced in the afternoon with improvement by the morning. He is a lawyer in California and does not smoke. He has no pets, has not traveled outside the country recently, and has had no sick contacts over this period. His father recently had a stroke, so the patient helps him manage his farm on the weekends. The patient has a temperature of 37.2°C, blood pressure of 128/84 mmHg, heart rate of 82 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 99% on room air. His physical examination is unremarkable. A chest x-ray is normal, and the patient elects to undergo lung biopsy that reveals multiple noncaseating interstitial granulomas.

What is the most likely diagnosis?

- (A)** Chronic obstructive pulmonary disease
- (B)** Sarcoidosis
- (C)** Hypersensitivity pneumonitis
- (D)** Silicosis
- (E)** Coccidioidomycosis
- (F)** Tuberculosis

**The answer is C: Hypersensitivity pneumonitis.** The temporal relationship of symptoms during weekends, along with the history of visiting a farm on weekends, suggests hypersensitivity pneumonitis as the diagnosis. There are three forms of the disease: acute, subacute, and chronic. This patient likely has the acute form, which presents with symptoms such as fevers, chills, chest tightness, and dyspnea usually 4 to 6 hours after exposure to the organic dust (compared to *inorganic dusts* in pneumoconiosis). “Farmer’s lung” is one of the most common causes of hypersensitivity pneumonitis and is caused by a variety of agents (e.g., thermophilic actinomycetes). Other important exposures that

may cause hypersensitivity pneumonitis include birds and other animals, plant products from lumber milling, and ventilation sources. The most important treatment is avoidance of exposure to the etiologic antigen.

Hypersensitivity pneumonitis is distinct from the other environmental exposures termed pneumoconiosis. Important pneumoconiosis include asbestosis (shipbuilders, textile workers, construction workers with pleural plaques and increased risk of cancer), silicosis (miners, sand blasters with eggshell calcifications and increased risk of TB and cancer), berylliosis (machine and metal workers with a chronic granulomatous disease that mimics sarcoidosis), and coal worker's pneumoconiosis (nodularity like silicosis with risk for massive pulmonary fibrosis).

(A) This patient has no history of smoking and has intermittent symptoms with a normal chest x-ray, making COPD a less likely diagnosis. (B) Sarcoidosis is a granulomatous disease most commonly affecting the lungs, and noncaseating granulomas would be seen on biopsy; however, the intermittent nature of the symptoms does not fit with sarcoidosis. Bilateral hilar lymphadenopathy is also frequently seen on chest x-ray. (D) Silicosis is caused by inhalation of silica, which is not suggested by this patient's occupational history. (E) Coccidioidomycosis is caused by the dimorphic fungus *Coccidioides immitis*. There would be no temporal relationship of the symptoms to weekends with this infection. (F) There is no exposure history that is suggestive of tuberculosis.

10

A 33-year-old man presents to the hospital complaining of dyspnea. Over the past year he has had increasing shortness of breath while running that limits the distance he can run. In addition, he has a persistent cough that is bothering him, and during the past few days he has had increasing sputum production that was previously white and is now yellow. He has not visited a doctor yet because he does not have medical insurance. The patient denies any significant medical history but has a positive family history of emphysema. He smokes half a pack of cigarettes daily and drinks alcohol moderately. On examination, he has a temperature of 37.9°C, blood pressure of 122/76 mmHg, heart rate of 93 beats per minute, respiratory rate of 24 breaths per minute, and oxygen saturation of 92% on room air. He has scattered wheezes throughout both lung fields with a normal cardiac examination. A chest x-ray shows loss of interstitial lung markings primarily at the lung bases.

Which of the following is the mechanism by which this disease produces liver disease?

- (A) Failure to inhibit the destruction of connective tissue by elastase
- (B) Pulmonary artery hypertension leading to increased pressure in the hepatic vein
- (C) Direct hepatic injury resulting in Mallory bodies
- (D) Accumulation of abnormal proteins within hepatocytes

**The answer is D: Accumulation of abnormal proteins within hepatocytes.** For a young patient presenting with symptoms and signs of COPD, always consider  $\alpha_1$ -antitrypsin deficiency as the cause. Although this autosomal recessive disease usually presents in patients after the age of 40, it can present earlier if the patient is a smoker.  $\alpha_1$ -Antitrypsin is a protease inhibitor that is produced in the liver and inhibits elastase in the lungs. During acute inflammation, neutrophils release elastase in the lungs that can degrade elastin, an important structural protein that helps tissues maintain their shape. Normally this is inhibited by  $\alpha_1$ -antitrypsin; however, patients with  $\alpha_1$ -antitrypsin deficiency will develop panacinar emphysema due to unopposed destruction of elastin in the lung parenchyma. If a patient is exposed to greater than average amounts of toxins (e.g., smoking) that produce lung injury and inflammation, they will develop manifestations of emphysema at a younger age. The clues to the diagnosis in this case are the fact that the patient is very young, has a family history of emphysema, and has emphysema that is predominantly affecting the lung bases (seen on chest x-ray).

Another clue is that the question stem states that liver disease is associated with the condition. Not all mutations cause liver disease, but some genotypes lead to the production of an abnormal protein within hepatocytes that polymerizes and causes cell apoptosis. (A) Therefore, the mechanism of liver disease is different from the mechanism of lung disease, with connective tissue destruction not being a prominent feature. When the liver is biopsied, the cytoplasmic inclusions are periodic acid-Schiff positive. Skin findings (e.g., necrotizing panniculitis) are another extrapulmonary manifestation that may be associated with this disease. Diagnosis of  $\alpha_1$ -antitrypsin deficiency is made by finding low serum levels of  $\alpha_1$ -antitrypsin as well as genotyping the patient. Treatments include smoking cessation, IV supplementation of  $\alpha_1$ -antitrypsin, standard treatments for COPD based on severity of disease, and lung or liver transplant if end-stage disease is present.

(B) Emphysema causes pulmonary vascular destruction, which can lead to increased pulmonary artery pressure and eventually cor pulmonale. Congestive hepatopathy as a result of elevated venous pressure would exacerbate the liver disease, but it is not the primary cause of the liver disease in  $\alpha_1$ -antitrypsin deficiency. (C) Mallory bodies are cytoplasmic inclusions seen within hepatocytes in alcoholic liver disease. They are not 100% specific to alcoholic liver disease and may rarely be seen on histology in  $\alpha_1$ -antitrypsin deficiency. However, this is not the best explanation for the mechanism of liver disease in these patients.

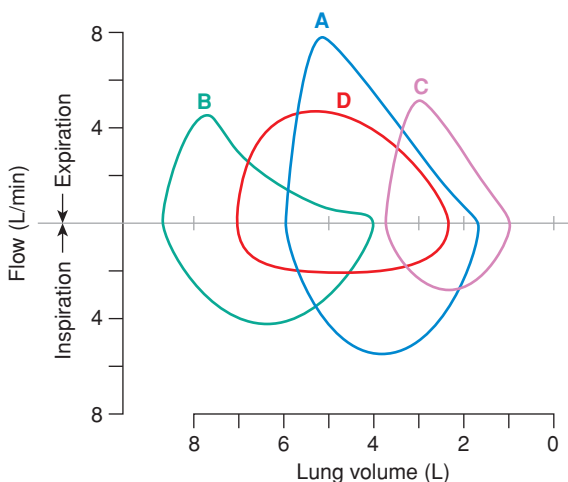


11 A 62-year-old man presents to the clinic with dyspnea on exertion. He reports a progressive decline in his exercise tolerance over the last few years, and complains that he feels like he is always coughing up white mucus. He denies any fever, weight loss, hemoptysis, chest pain, or leg swelling. His medical history is significant for hyperlipidemia and



GERD, for which he takes atorvastatin and omeprazole. He has smoked a pack of cigarettes daily for the past 40 years. He is afebrile with normal vitals. On examination, he has decreased breath sounds with a prolonged expiratory phase and scattered wheezes. There is hyper-resonance to percussion in bilateral lung fields. The rest of the examination is unremarkable, and he is referred for further testing with spirometry.

Which of the following represents the likely flow-volume loop in this patient (*Figure 2-1*)?



**Figure 2-1**

- (A) Option A
- (B) Option B
- (C) Option C
- (D) Option D

**The answer is B: Option B.** COPD is a common condition resulting from chronic inflammation of the airways leading to progressive airflow limitation. Most cases occur in older patients and are the result of chronic smoking; in a young patient without a significant smoking history, consider other causes (such as  $\alpha_1$ -antitrypsin deficiency). There are two processes that typically occur in COPD: emphysema (a histopathologic finding) and chronic bronchitis (a clinical finding). The type of emphysema seen on histology is centrilobular, whereas in  $\alpha_1$ -antitrypsin deficiency it is panacinar. Emphysema is the result of parenchymal destruction from chronic inflammation, which creates enlarged airspaces. With the loss of the supporting connective tissue, the lungs lose their elastic recoil and the airspaces enlarge, creating high lung volumes; in addition, small airways collapse during expiration due to a loss of tethering that the connective tissue provides, which causes air trapping and further expansion

in lung volumes. This affects respiratory function by decreasing both ventilation and perfusion via destruction of airspaces and vasculature, leading to mild hypoxemia.

Chronic bronchitis is defined as having a productive cough for more than 3 months of the year for at least 2 years. Inflammation of small airways causes narrowing and excessive sputum production leading to increased airway resistance and a prolonged expiratory phase. This causes V/Q mismatch and hypoxemia. The end result of both emphysema and chronic bronchitis is high lung volumes with increased compliance (large changes in volume based on small changes in pressure, the opposite of elasticity), leading to increased dead space during ventilation and chronic hypoxemia.

This patient presents with classic symptoms of dyspnea on exertion and chronic productive cough, with physical findings highly suggestive of COPD. Spirometry is required to make the diagnosis (decreased FEV<sub>1</sub>/FVC ratio), as not all patients will have the classic symptoms noted above. When flow-volume loops (spirograms) are constructed, there is a classic “scooped-out” appearance during expiration in obstructive lung diseases like COPD. This is caused by the pathologic changes in the airways in which the expiratory flow rapidly decreases due to loss of elastic recoil, increased airway resistance, and collapse of small airways. **(A)** This is a normal flow-volume loop. **(C)** With restrictive lung diseases, the flow-volume loop is smaller and shifted to the right. This is caused by an increase in elastic recoil of the lung leading to decreased lung volumes. **(D)** In patients with a fixed upper airway obstruction (e.g., subglottic stenosis), there is a limit to the airflow that can be generated during inspiration and expiration because of the fixed narrowing of the airway. This is seen as a plateau in the flow-volume loop.

**12** A 42-year-old woman presents with progressive fatigue over the past few weeks. She reports muscle fatigue, occasional double vision, and some difficulty breathing. She has no relevant past medical history and takes no medications. On examination, sustained upward gaze leads to muscle fatigue and bilateral ptosis. Pulmonary function testing is performed and is shown below.

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| FEV <sub>1</sub>                                          | 85% of predicted  |
| Forced vital capacity (FVC)                               | 85% of predicted  |
| FEV <sub>1</sub> /FVC                                     | 105% of predicted |
| Total lung capacity (TLC)                                 | 70% of predicted  |
| Diffusion capacity of the lung for carbon monoxide (DLCO) | 100% of predicted |

Which of the following is responsible for this patient's pattern on pulmonary function testing?

- (A) Chronic obstructive pulmonary disease
- (B) Neuromuscular disease
- (C) Pulmonary fibrosis
- (D) Pulmonary hemorrhage

**The answer is B: Neuromuscular disease.** Myasthenia gravis is a neuromuscular disease caused by autoantibodies directed against postsynaptic acetylcholine receptors. Neuromuscular diseases can show a restrictive pattern (decreased FEV<sub>1</sub> and FVC but normal/increased FEV<sub>1</sub>/FVC ratio) on pulmonary function testing that is extrinsic to the lung itself and therefore will have a normal DLCO. Examples include lower motor neuron disease (e.g., polio and Guillain-Barré syndrome), myasthenia gravis, Lambert-Eaton syndrome, muscular dystrophies, chest wall deformities (e.g., scoliosis and pectus carinatum), and obesity.

(A) COPD will present with an obstructive pattern on spirometry (decreased FEV<sub>1</sub>/FVC ratio) with a decreased DLCO (if there is a prominent component of emphysema). (C) Pulmonary fibrosis is a type of interstitial lung disease, which will show a restrictive pattern on spirometry as well as a decreased DLCO from parenchymal destruction and scarring. (D) Pulmonary hemorrhage would present with normal spirometry but an *increased* DLCO, since the presence of red blood cells within the airways will cause a rapid consumption of carbon monoxide during the test.

13

A 68-year-old woman with a history of hypothyroidism and COPD presents for follow-up with her primary care physician. She has no complaints and denies any recent fatigue, weight loss, increase in cough or sputum production, or chest pain. Her medications include inhaled ipratropium and levothyroxine. She is normotensive with an SaO<sub>2</sub> of 92% on room air. On examination, her lungs are hyper-resonant to percussion with some scattered wheezes and rhonchi. She has clubbing of the digits, which was not present 1 year ago.

What is the most appropriate next course of action?

- (A) Reassurance and regular follow-up
- (B) Home oxygen therapy
- (C) Pulmonary function tests
- (D) Chest imaging

**The answer is D: Chest imaging.** Clubbing of the digits is not associated with COPD, and therefore any new onset of clubbing in a COPD patient is a red flag for another etiology such as bronchogenic carcinoma. Chest imaging is an important diagnostic step to look for cancer. Other etiologies of clubbing include interstitial lung disease, cystic fibrosis, congenital heart disease, and malabsorption. (A) Because the clubbing is unrelated to the patient's COPD,

reassurance is inappropriate. **(B)** This patient does not meet criteria for home oxygen therapy ( $\text{SaO}_2 \leq 88\%$ ). **(C)** The patient is not having an exacerbation and has no reason to undergo pulmonary function testing at this time.

**14** A 46-year-old man with a history of ulcerative colitis is admitted to the hospital with abdominal pain and heavy rectal bleeding. Initial laboratory samples are drawn, and his hemoglobin is measured at 6 g/dL. He is given IV methylprednisolone and 2 units of packed red blood cells. Three hours later, the patient complains of shortness of breath and is given supplemental oxygen at an  $\text{FiO}_2$  of 30%. He appears anxious and is gasping for breath while speaking. There is no jugular venous distention or murmurs on cardiac examination. An arterial blood gas shows a  $\text{PaO}_2$  of 55 mmHg and a  $\text{PaCO}_2$  of 36 mmHg. A chest x-ray shows fluffy opacities in both lung fields with a normal cardiac silhouette.

What intervention should be performed next?

- (A)** Transfuse more units of packed red blood cells
- (B)** Diuresis with furosemide
- (C)** Intubation and positive end-expiratory pressure (PEEP)
- (D)** Plasmapheresis

**The answer is C: Intubation and positive end-expiratory pressure (PEEP).** A  $\text{PaO}_2/\text{FiO}_2$  ratio  $\leq 200$  with pulmonary edema that is noncardiogenic – no jugular venous distention or elevated pulmonary capillary wedge pressure (PCWP) – meets criteria for acute respiratory distress syndrome (ARDS). The most common causes of ARDS are pneumonia, sepsis, and aspiration. The pathophysiology involves alveolar and capillary endothelial injury, which causes a strong inflammatory response and leakage of fluid into the lungs. This patient developed ARDS within 6 hours of a transfusion, making the most likely diagnosis transfusion-related acute lung injury (TRALI). Despite the name, TRALI can present with acute lung injury or ARDS. The management of ARDS involves intubation with mechanical ventilation targeting low tidal volumes and increased PEEP to help prop open alveoli for gas exchange.

**(A)** This patient suffered TRALI and therefore no more transfusions should be given at this time. However, patients that experience one episode of TRALI are not necessarily at an increased risk of TRALI in the future. **(B)** Hypervolemia can increase fluid leakage from damaged capillaries in the lung during ARDS. This patient is likely hypovolemic due to the heavy blood loss from ulcerative colitis, and therefore diuresis is not a good answer choice. **(D)** There is no role for plasmapheresis in ARDS or TRALI specifically.

**15** A 52-year-old man presents to his physician with complaints of cough and difficulty breathing during exercise. He also endorses weight loss and night sweats that he noticed over the past few months. The

patient has a history of diabetes and takes metformin. He works at a stone quarry, does not smoke or drink alcohol, and does not use any illicit drugs. A chest x-ray shows multiple small nodules in the upper lobes of each lung and multiple areas of calcification around lymph nodes.

Which of the following is the most appropriate next step in management?

- (A) Measure serum angiotensin-converting enzyme
- (B) Systemic corticosteroids
- (C) Administer a tuberculin skin test
- (D) Lung biopsy

**The answer is C: Administer a tuberculin skin test.** The diagnosis of silicosis is made by taking a history concerning for silica exposure, obtaining chest imaging that is consistent with silicosis, and ruling out other diseases that may mimic silicosis. Common environmental exposures to silica include stone quarries, mining, sand blasting, and construction. Chest imaging is somewhat variable based on the type of presentation (acute, chronic, or accelerated); however, it will typically show small nodules within the upper lobes. There may also be calcifications around lymph nodes (“eggshell calcifications”). Buzzwords like eggshell calcifications are good to know, but the test does not always give the buzzwords and may instead describe the findings!

Patients with silicosis may be asymptomatic or may present with cough and dyspnea on exertion. They are at an increased risk for tuberculosis, and therefore patients with a diagnosis of silicosis should undergo tuberculin skin testing with purified protein derivative (PPD). They are also at an increased risk of lung cancer, similar to other pneumoconiosis. (A) Elevated ACE may be seen in sarcoidosis, but this patient’s occupational history and chest x-ray suggest silicosis as the diagnosis. (B) Preventive therapy is the key in pneumoconiosis, and treatment after silicosis develops is typically based on symptom management. There are mixed results about the usefulness of glucocorticoids in the treatment of silicosis. (D) Additional workup is not necessary to make the diagnosis of silicosis.

16

A 59-year-old woman with a previous diagnosis of bladder cancer, diabetes, and coronary artery disease presents to the hospital with fevers, chills, and right flank pain. She is hypotensive; empiric antibiotics are started and a central line is placed for heavy fluid resuscitation. Her temperature is 39.3°C and blood pressure is 65/40 mmHg. An arterial blood gas shows a PaO<sub>2</sub> of 80 mmHg on supplemental oxygen with a face mask set to a fraction of inspired oxygen of 50%. A chest x-ray is ordered and shows bilateral fluffy infiltrates. A pulmonary artery catheter is advanced and records a PCWP of 22 mmHg.

Which of the following is the most likely diagnosis?

- (A) Anaphylaxis
- (B) Acute lung injury (ALI)
- (C) Acute respiratory distress syndrome (ARDS)
- (D) Heart failure

**The answer is D: Heart failure.** The findings of pulmonary edema with an elevated PCWP suggest that this patient has cardiogenic shock. The original presentation of pyelonephritis is not particularly important in answering the question, but it is likely from urinary obstruction given her history of bladder cancer. The reader's goal here is to differentiate between cardiogenic and non-cardiogenic causes of acute pulmonary edema. (C) ARDS is a potential complication of sepsis and has a high mortality. It is defined as an acute process that meets the following criteria: bilateral pulmonary infiltrates on chest imaging, severe hypoxemia ( $\text{PaO}_2/\text{FiO}_2$  ratio  $\leq 200$ ), and normal cardiac pressures (no jugular venous distention or a PCWP  $< 18$  mmHg). Although this is a tempting answer choice, the PCWP was 22 mmHg, indicating a high left atrial pressure that is not consistent with ARDS alone; therefore a cardiac etiology should be suspected. Cardiac failure is also a consequence of sepsis, and will present with hypotension and pulmonary edema. The take home point here is to make sure the pulmonary edema is noncardiac in nature when diagnosing ARDS. (B) ALI is a milder process on the spectrum leading to ARDS, and is diagnosed with the finding of a  $\text{PaO}_2/\text{FiO}_2$  ratio  $\leq 300$  but  $> 200$ . This patient's ratio is calculated at  $80/0.5 = 160$ , and thus she would not meet the definition of ALI. (A) Anaphylaxis is a form of distributive shock that would primarily be a consequence of decreased systemic vascular resistance. The PCWP would not be elevated.

**17** An 18-year-old girl is brought in to the hospital by her parents because of an asthma attack. She normally takes inhaled fluticasone and albuterol; however, she is not currently responding to the albuterol. On examination, she appears anxious and is moderately short of breath. There are loud bilateral wheezes on examination, with a prolonged inspiratory and expiratory phase and use of accessory muscles of respiration. Her temperature is  $37.6^\circ\text{C}$ , blood pressure is 118/78 mmHg, heart rate is 106 beats per minute, respiratory rate is 26 breaths per minute, and oxygen saturation is 93% on room air. She is placed on supplemental oxygen and bronchodilators and an arterial blood gas is drawn.

#### Arterial Blood Gas

|                 |         |
|-----------------|---------|
| pH              | 7.40    |
| $\text{PaO}_2$  | 60 mmHg |
| $\text{PaCO}_2$ | 40 mmHg |

Which of the following is the most appropriate next step in management?

- (A) Increase supplemental oxygen flow rate
- (B) IV corticosteroids
- (C) Azithromycin
- (D) Intubation

**The answer is D: Intubation.** The patient in this vignette is experiencing an acute asthma exacerbation with worrisome symptoms/signs: loud wheezes, use of respiratory accessory muscles, tachycardia, tachypnea, and poor oxygen saturation. In addition, the arterial blood gas shows a normal  $\text{PaCO}_2$ , which is not a good sign; hypoxic patients should hyperventilate to maintain oxygenation, which causes hypocapnia and a respiratory alkalosis. When a patient has a normal  $\text{PaCO}_2$ , this is a sign that the patient is tiring and decompensating. Even though intubation should be avoided if possible, there is a low threshold for intubating patients that are showing signs of respiratory fatigue. (A) Increasing the oxygen flow rate might improve oxygenation, but the patient is likely starting to develop hypercapnic respiratory failure, which is due to inadequate ventilation. Once the patient is on a ventilator, ventilation is controlled primarily by adjusting the respiratory rate or tidal volume. Oxygenation can be maintained by adjusting the  $\text{FiO}_2$  and positive end-expiratory pressure (PEEP). (B) IV corticosteroids are used in acute exacerbations but will not act immediately to prevent this patient from further decompensation. (C) Azithromycin and other antibiotics are used in acute COPD exacerbations, not acute asthma exacerbations.

18

A 24-year-old man presents to the hospital after coughing up blood. He developed a fever and a worsening cough over the past few days, with sputum that was originally yellow but became bloody this morning. Further history reveals that the patient has recurrent sinus infections and a chronic productive cough. He moved to the United States from Russia when he was 3 and has had regular medical care since that time. He is adopted and does not know his family history, and he does not smoke or use any illicit drugs. On examination, he is febrile and tachycardic. There are loud wheezes and rhonchi heard over the upper lobes bilaterally. Laboratory values are notable for a glucose of 145 mg/dL, and sputum culture is positive for *Pseudomonas*.

Which of the following findings would most likely be seen on a CT scan?

- (A) Fluid within the paranasal sinuses with surrounding bone and soft tissue destruction
- (B) Dilated bronchi with wall thickening and mucus plugging
- (C) Lobar consolidation with air bronchograms
- (D) Bilateral hilar lymphadenopathy

**The answer is B: Dilated bronchi with wall thickening and mucus plugging.** Recurrent sinopulmonary infections in a patient with an unknown family history is concerning for a possible underlying diagnosis of cystic fibrosis. In patients that present after the age of 20 due to less severe mutations in the CFTR gene, the most common manifestation is pulmonary disease (recurrent sinus infections and bronchiectasis). Other symptoms that suggest cystic fibrosis, such as diabetes or malabsorption from pancreatic insufficiency, are not as common in patients that present after the age of 20. *Pseudomonas* is a common colonizer in the respiratory tracts of these patients and causes recurrent infections. This patient likely has underlying bronchiectasis and is experiencing an acute exacerbation from *Pseudomonas* infection. A high-resolution CT will show findings of bronchiectasis: dilatation of airways with bronchial wall thickening and mucus plugging with atelectasis. Treatment with antibiotics should be initiated. Other treatments that may be useful in cystic fibrosis include  $\beta_2$  agonists, inhaled hypertonic saline, dornase alfa (DNase to reduce viscosity of secretions), and preventive therapy with macrolide antibiotics.

(A) Mucormycosis is a necrotizing sinus infection seen in diabetics that rapidly spreads to the brain and is often fatal. It is caused most often by fungal species of *Mucor* and *Rhizopus*, not by the bacteria *Pseudomonas*. The patient has hyperglycemia, but a diagnosis of diabetes is not confirmed (we do not know if this is a fasting value). In addition, the physical examination did not report any erythema or necrosis of the skin around the nose, which may be seen in mucormycosis. (C) Lobar consolidation with air bronchograms is seen in lobar pneumonia; however, this is not necessarily the case in this patient (he might just have a local infection or exacerbation of bronchitis). Therefore, the better answer is (B): CT findings of bronchiectasis. (D) Bilateral hilar lymphadenopathy is suggestive of sarcoidosis and is not a prominent feature of bronchiectasis.



19 An older woman with a long history of smoking presents with hypercalcemia and is eventually diagnosed with lung cancer.

Which of the following types of lung cancer is most associated with this presentation?

- (A) Small cell lung cancer
- (B) Adenocarcinoma
- (C) Large cell carcinoma
- (D) Squamous cell carcinoma
- (E) Bronchioloalveolar carcinoma

**The answer is D: Squamous cell carcinoma.** Hypercalcemia from tumor production of parathyroid hormone-related protein (PTHrP) is a potential paraneoplastic syndrome associated with certain types of lung cancer. PTHrP acts similarly to endogenous PTH to increase serum calcium and decrease serum phosphate. The most common type of cancer associated with the release of PTHrP is squamous cell carcinoma, which can be remembered with



the mnemonic “sCa<sup>2+</sup>mous.” (B, D) Adenocarcinoma and small cell lung cancer can both produce PTHrP, but this occurs less often than with squamous cell carcinoma. Adenocarcinomas are also associated with hypertrophic osteoarthropathy (clubbing and periosteal proliferation of long bones) and a propensity to form clots. Small cell lung cancer is associated with many paraneoplastic syndromes, including ectopic ACTH production (Cushing syndrome), SIADH, and Lambert–Eaton syndrome. (C) Large cell carcinoma is a rare tumor of the lung that tends to be located peripherally and does not produce PTHrP. (E) Bronchioloalveolar carcinomas are typically found in nonsmokers and are associated with EGFR mutations.

20

A 42-year-old woman comes to the physician with symptoms of suprapubic discomfort, dysuria, and frequency. Her urinalysis suggests a urinary tract infection (UTI), and she is given a prescription for ciprofloxacin. Before she leaves, you notice some abnormalities in the patient's vitals. She is afebrile with a blood pressure of 162/96 mmHg, heart rate of 86 beats per minute, respiratory rate of 19 breaths per minute, and oxygen saturation of 90% on room air. On examination, the patient is obese with a BMI of 49 kg/m<sup>2</sup> and does not appear short of breath. She has distant heart and lung sounds, with a few faint crackles heard at the bases. An electrolyte panel is drawn, which is significant for a bicarbonate level of 32 mEq/L. An arterial blood gas is drawn and shows a pH of 7.35, PaO<sub>2</sub> of 65 mmHg, and PaCO<sub>2</sub> of 60 mmHg. Upon further questioning, the patient admits to daytime fatigue and loud snoring at night.

In addition to the UTI, what other diagnosis does this patient likely have that can explain her laboratory abnormalities?

- (A) Flash pulmonary edema from hypertension
- (B) Obstructive sleep apnea
- (C) Obesity hypoventilation syndrome
- (D) Pulmonary embolism

**The answer is C: Obesity hypoventilation syndrome.** The main clues to this diagnosis are the following: the patient is obese, not short of breath on examination, and has evidence of chronic hypoxemia and hypercapnia measured during the daytime. These findings suggest obesity hypoventilation syndrome (Pickwickian syndrome), a disease in which there is no direct lung pathology but rather there is a problem of inadequate ventilation (therefore, the A–a gradient will be normal). The pathophysiology is multifactorial, with components of an increased work of breathing with chronic respiratory muscle fatigue, V/Q mismatch, and decreased central ventilatory drive. Besides lifestyle modifications, all patients should start noninvasive positive airway pressure during the night with either continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP). This will decrease the

work of respiration while improving ventilation and therefore normalize the PaCO<sub>2</sub> (both during the night and during the day). CPAP is preferred to BiPAP initially if the patient also has obstructive sleep apnea.

(B) Obesity hypoventilation syndrome and obstructive sleep apnea are often comorbid conditions. While obstructive sleep apnea is suggested by the patient's snoring, daytime fatigue, and hypertension, this would not produce daytime hypoxemia and hypercapnia and therefore is not the best answer. (A) Flash pulmonary edema is an acute process that produces dyspnea. This patient is asymptomatic and the crackles heard on examination are likely from atelectasis (common in obese patients). (D) This patient does not have tachycardia or tachypnea and is not acutely symptomatic, making pulmonary embolism less likely.



21 A 29-year-old woman with a history of asthma presents with progressive worsening of respiratory function. She reports that her symptoms have developed gradually over the past few months, with occasional fevers and episodes of mild hemoptysis. She denies any weight loss, skin changes, or diarrhea. Her medications include inhaled albuterol as needed and OCPs. She has no family history of cancer, no recent travel, and no recent sick contacts. She works as an accountant and does not smoke or use any illicit drugs. On examination, she has a low-grade fever with scattered wheezes and rhonchi over bilateral lung fields. After coughing vigorously, a brown mucus plug is expectorated. Her laboratory values show eosinophilia with an elevated total serum IgE. A chest x-ray shows interstitial infiltrates in the upper lobes with some areas of atelectasis bilaterally, and a CT scan shows enlarged airways primarily in the upper lobes with bronchial wall thickening.

Which of the following is the most likely diagnosis?

- (A) Tuberculosis
- (B) *Pseudomonas aeruginosa*
- (C) *Strongyloides stercoralis*
- (D) Allergic bronchopulmonary aspergillosis
- (E) Bronchial carcinoid tumor
- (F) Worsening asthma

**The answer is D: Allergic bronchopulmonary aspergillosis.** The key to answering this question is knowing what conditions are associated with an underlying diagnosis of asthma. Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity reaction to *Aspergillus* colonization in the bronchi. These patients may develop worsening respiratory function with hemoptysis, and can eventually develop bronchiectasis, which was seen on this patient's CT scan. Be suspicious about this diagnosis in patients with asthma, peripheral eosinophilia, and elevated IgE, and imaging findings of lung infiltrates and bronchiectasis. Diagnosis is further suggested by a skin prick test to assess for

reactivity to *Aspergillus* antigens. Treatment is with systemic glucocorticoids and itraconazole.

Other important associations with asthma include aspirin allergy (asthma with sensitivity to aspirin and nasal polyps), Churg–Strauss (asthma with vasculitis), and the atopic triad (asthma with eczema and allergic rhinitis). (A) The patient has no risk factors for tuberculosis, and this would not present with eosinophilia and enlarged airways (chronic untreated tuberculosis could cause airway destruction and bronchiectasis, but an acute infection would not). (B) *Pseudomonas* is a common cause of pulmonary infection in cystic fibrosis patients, but this patient lacks other findings that suggest cystic fibrosis (pancreatic insufficiency, family history, etc.). (C) *Strongyloides stercoralis* is a parasitic nematode that can penetrate the skin and migrate to the lungs, resulting in wheezing and coughing. Eosinophilia and elevated IgE may be seen in parasitic infections; however, she has no apparent risk factors for *S. stercoralis* and the CT scan is consistent with ABPA, not *S. stercoralis* infection. (E) Carcinoid syndrome is caused by a neuroendocrine tumor that is usually in the GI tract or bronchus. There is a lower rate of carcinoid syndrome in bronchial tumors than in GI tumors due to less production of serotonin and other vasoactive amines. Other symptoms of carcinoid syndrome include cutaneous flushing and diarrhea. (F) Infiltrates and bronchiectasis on imaging cannot be explained solely by worsening asthma.

22

A 52-year-old man is hospitalized for an acute COPD exacerbation and agrees to treatment with 3 days of IV methylprednisolone followed by a taper of oral prednisone over 10 days.

Which of the following is this patient most likely to experience as a potential adverse effect of these medications?

- (A) Muscle pain and weakness
- (B) Serious infections
- (C) Skin atrophy and purpura
- (D) Psychiatric disturbances
- (E) Hypertension
- (F) Hyperglycemia
- (G) Osteoporosis
- (H) Chronic adrenal suppression

**The answer is F: Hyperglycemia.** Systemic corticosteroids have a long list of adverse effects when used chronically; however, there is debate as to the frequency of adverse effects when used over a short period of time. All of the answer choices are potential consequences of chronic therapy, but the one answer choice that most commonly occurs with a short course of steroids is hyperglycemia. Other notable side effects of chronic steroids (i.e., iatrogenic Cushing syndrome) are cataracts, dyslipidemia, pancreatitis, hypokalemia, and VZV reactivation (herpes zoster).

23

A 59-year-old woman with a history of hypertension and COPD presents to the hospital with shortness of breath. She recently visited her grandchildren and noticed several days later that her chronic cough became worse with an increase in yellow sputum production. She has also had to decrease her activities because of worsening dyspnea with any exertion. Her medications include hydrochlorothiazide, tiotropium, and inhaled albuterol and ipratropium as needed. She has a temperature of 37.6°C, blood pressure of 138/88 mmHg, heart rate of 96 beats per minute, respiratory rate of 28 breaths per minute, and oxygen saturation of 87% on room air. She is anxious and is using respiratory accessory muscles to breathe. There is hyper-resonance to percussion along both lung fields with wheezes and rhonchi heard bilaterally. Cardiac examination, as well as the rest of the physical examination, is unremarkable. The patient is admitted and her chest x-ray is shown in *Figure 2-2*.



**Figure 2-2**

Which of the following is NOT an appropriate first-line treatment for the patient at this time?

- (A) Oxygenation
- (B) Methylprednisolone
- (C) Amoxicillin
- (D) Inhaled corticosteroids

**The answer is D: Inhaled corticosteroids.** This patient is presenting with a history of COPD with an acute exacerbation, which is defined as an increase in any of the chronic symptoms of COPD (increased frequency/severity of cough, increased dyspnea, or increased sputum amount or change in color). The majority of acute exacerbations are caused by respiratory infections, with common etiologies including viruses, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, and *Pseudomonas aeruginosa*. Any other process involving the lungs can cause an exacerbation, including heart disease, environmental/toxic exposures, and pulmonary embolism. The chest x-ray above shows hyperinflated lungs with flattening of the diaphragm and elongation of the heart border, which is consistent with her diagnosis of COPD.

(A, B, C) Management of acute COPD exacerbations should be differentiated from the management of chronic disease. Important therapies during an exacerbation include oxygen administration targeting an  $\text{SaO}_2$  of 90% to 94% (dependent on whether or not they are a chronic  $\text{CO}_2$ -retainer), inhaled bronchodilators (anticholinergics and  $\beta_2$  agonists), systemic corticosteroids (prednisone or methylprednisolone), and antibiotics. Antibiotics such as amoxicillin show some benefit in COPD exacerbations, although the type of antibiotic does not matter unless a specific organism can be targeted. (D) Although inhaled corticosteroids are useful in the chronic treatment of COPD, there is no evidence for their use in acute exacerbations and should not be used instead of systemic corticosteroids.

24

A 29-year-old man is diagnosed with testicular cancer and undergoes orchiectomy. He is followed afterward, and the cancer recurs. He elects to undergo treatment with bleomycin, etoposide, and cisplatin for four cycles. Several months after finishing chemotherapy, he returns for follow-up. On examination, he has bilateral dry crackles over both lung fields. His laboratory values are significant for a hemoglobin of 9.4 g/dL and a creatinine of 2.4 mg/dL (baseline 1.1 mg/dL).

Which of the following is most likely responsible for the lung findings on examination?

- (A) Tumor metastases
- (B) Bleomycin
- (C) Etoposide
- (D) Cisplatin

**The answer is B: Bleomycin.** Bleomycin is an antineoplastic antibiotic used in the treatment of many cancers including testicular cancer, Hodgkin lymphoma, and squamous cell carcinomas. A very common and important adverse effect of this drug is pulmonary fibrosis, which is concerning in this patient given the diffuse dry crackles on lung examination. Other adverse

effects include hepatotoxicity and nephrotoxicity. This patient also has anemia and renal failure, which are potential adverse effects of all three of the antineoplastic drugs in the answer choices. It is important to remember the other iatrogenic causes of pulmonary fibrosis, which include amiodarone, thiazides, isoniazid, cyclophosphamide, methotrexate, and radiation therapy. (A) Tumor metastases to the lungs would not cause the findings on examination in this patient. (C) Etoposide is another antineoplastic drug that acts as a topoisomerase inhibitor with adverse effects including congestive heart failure and Stevens–Johnson syndrome. (D) Cisplatin is a platinum-based antineoplastic drug with important toxicities that include neuropathy and nephrotoxicity.

25

A 57-year-old woman presents to the hospital with shortness of breath. Her medical history is significant for seasonal allergies and hypertension, with no personal or family history of heart disease. She has smoked 2 packs of cigarettes daily for the past 20 years. During hospitalization, she is treated with oxygen, steroids, and bronchodilators. She is discharged and follows up as an outpatient to get pulmonary function tests, which are shown below.

---

FEV<sub>1</sub>

|                  |                  |
|------------------|------------------|
| Before albuterol | 70% of predicted |
|------------------|------------------|

|                 |                  |
|-----------------|------------------|
| After albuterol | 76% of predicted |
|-----------------|------------------|

---

|     |                  |
|-----|------------------|
| FVC | 89% of predicted |
|-----|------------------|

---

|                       |      |
|-----------------------|------|
| FEV <sub>1</sub> /FVC | 0.60 |
|-----------------------|------|

---

|                           |                   |
|---------------------------|-------------------|
| Total lung capacity (TLC) | 110% of predicted |
|---------------------------|-------------------|

---

|      |                  |
|------|------------------|
| DLCO | 85% of predicted |
|------|------------------|

---

Which of the following is the most likely diagnosis?

- (A) Neuromuscular weakness
- (B) Asthma
- (C) Chronic obstructive pulmonary disease
- (D) Interstitial lung disease

**The answer is C: Chronic obstructive pulmonary disease.** It is very important to know how to interpret pulmonary function tests for the Internal Medicine shelf examination. This woman has a smoking history and

**Table 2-1** Obstructive and Restrictive Patterns on Pulmonary Function Testing

|                       | Obstructive Lung Disease | Restrictive Lung Disease |
|-----------------------|--------------------------|--------------------------|
| FEV <sub>1</sub>      | Low                      | Normal/slightly low      |
| FEV <sub>1</sub> /FVC | Low                      | Normal/high              |
| Peak expiratory flow  | Low                      | Normal                   |
| Total lung capacity   | High                     | Low                      |
| Vital capacity        | Low                      | Low                      |
| Residual volume       | High                     | Variable                 |

presented to the hospital with dyspnea that resolved with oxygen, bronchodilators, and steroids, making an obstructive lung disease a likely diagnosis. On spirometry, obstructive lung diseases will typically present with an FEV<sub>1</sub>/FVC ratio less than 0.70. Once this is established, asthma can be differentiated from COPD by administering a bronchodilator and seeing the response in FEV<sub>1</sub>. If the FEV<sub>1</sub> improves by >12%, then the diagnosis is asthma. This patient had an FEV<sub>1</sub> that improved by 6%, and therefore she has COPD. DLCO measures how much carbon monoxide diffuses into the blood after inhalation of a small sample. Diseases that decrease the functional surface area of gas exchange will have a decreased DLCO. This patient has a decreased DLCO, indicating that she has both a chronic bronchitis component as well as an emphysematous component, since the parenchymal destruction that accompanies emphysema will decrease the surface area for gas exchange and cause diffusion impairment. *Table 2-1* presents a summary to distinguish between obstructive and restrictive patterns on pulmonary function testing.

(A) Neuromuscular disorders can cause fatigue and hypercapnic respiratory failure. These patients will have a restrictive pattern on spirometry with a normal DLCO. (B) Asthma would be the correct answer if the patient's FEV<sub>1</sub> increased by >12% after albuterol, and the DLCO was normal. (D) Interstitial lung disease would present with a restrictive pattern and a decreased DLCO.

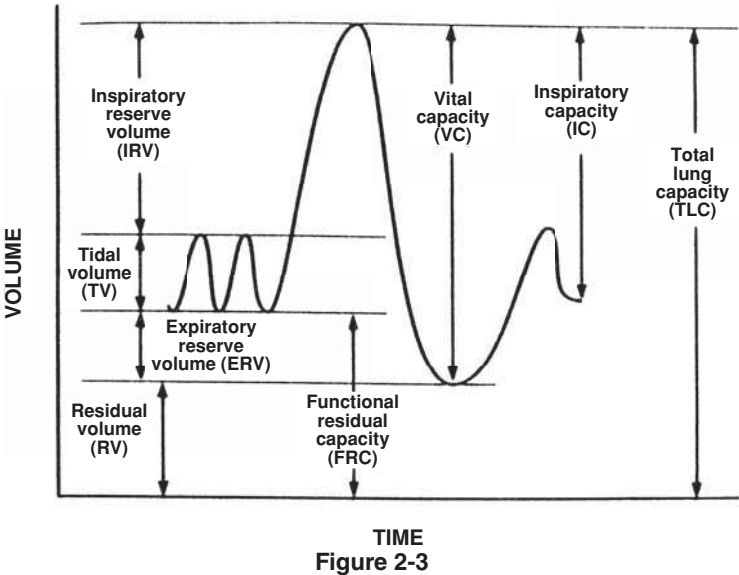
**26** A 70-year-old man presents to the clinic with a long history of chronic cough and shortness of breath. The cough is sometimes productive of white sputum in the morning, and he has decreased his level of exercise

over the years due to worsening shortness of breath. He has a 50 pack-year smoking history. On physical examination he has a large anterior-posterior diameter of his chest wall with hyper-resonance to percussion over the lung fields.

Compared to the lung volumes of a healthy patient, how would the lung volumes in this patient be different? (Note: VC is vital capacity, TLC is total lung capacity, RV is residual volume.)

|     | VC        | TLC       | RV        | RV/TLC Ratio |
|-----|-----------|-----------|-----------|--------------|
| (A) | Decreased | Increased | Increased | Increased    |
| (B) | Decreased | Increased | Increased | Decreased    |
| (C) | Decreased | Decreased | Decreased | Normal       |
| (D) | Normal    | Normal    | Normal    | Normal       |

**The answer is A: Decreased VC, Increased TLC, Increased RV, Increased RV/TLC Ratio.** This patient has COPD, a very common disease seen in older smokers as a result of chronic airway inflammation. Most patients have components of chronic bronchitis and emphysema. To answer questions like this on the examination, it is important to understand the components of lung volume (*Figure 2-3*).





Airway and parenchymal destruction from emphysema decreases the elastic recoil of the lung, allowing the chest wall to expand and increase the lung volumes (increased TLC). In addition, bronchioles are more collapsible during expiration as a result of the supporting connective tissue destruction that normally helps to prop open smaller airways. This causes air trapping and an increase in the RV. **(B)** The increase in RV is typically greater than the increase in TLC, making the RV/TLC ratio increased in these patients. **(C)** In restrictive lung diseases, there will be a relatively proportional decrease in all lung volumes, making the RV/TLC ratio normal. Examples include pulmonary fibrosis, in which scarring and contraction of the interstitium causes reduced volume; and neuromuscular disease, in which lung volumes are functionally reduced due to weakness of the muscles of respiration. **(D)** Lung volumes in a symptomatic COPD patient like this would not be normal.

**27**

A 32-year-old African American woman presents to the hospital with chest pain, cough, and difficulty breathing. Symptom onset has been gradual over the past few months. She has not traveled recently or been exposed to any sick contacts, and she has no personal or family history of cardiac disease. She works as an elementary school teacher and does not smoke or use illicit drugs. On examination, the patient is afebrile and her vitals are normal. The patient is admitted and a chest x-ray is obtained (*Figure 2-4*).



**Figure 2-4**

Which of the following laboratory values would most likely be elevated in this patient?

- (A) Serum potassium
- (B) Serum calcium
- (C) Rheumatoid factor
- (D) Angiotensin-converting enzyme
- (E) Reaction to tuberculin skin test

**The answer is D: Angiotensin-converting enzyme.** The risk of sarcoidosis is increased in African American patients, and is suggested by the development of chronic symptoms of chest pain, cough, and dyspnea. Sarcoidosis is a granulomatous disease that most commonly affects the lungs but can affect many other organs including the skin (granulomatous nodules, erythema nodosum), eyes (uveitis), heart (restrictive cardiomyopathy, conduction disturbances), nervous system (neurosarcoid), and more. The cause is unknown. Diagnosis can be made by putting together the clinical symptoms and risk factors, obtaining a chest x-ray that shows bilateral hilar adenopathy (*Figure 2-4*), and performing a biopsy that shows noncaseating granulomas. If pulmonary function tests are performed, a restrictive pattern may be seen.

Angiotensin-converting enzyme is produced in excess by granulomas within the lungs and is often elevated in these patients. However, its use in diagnosing sarcoidosis is limited by a high rate of false positives and false negatives. (A, B) Though hypercalcemia may be present, it is rare and a much less common finding than hypercalciuria. Hyperkalemia is not common. (C) Rheumatoid arthritis-associated lung disease typically presents as an interstitial process primarily affecting the lower lobes. (E) Testing for tuberculosis is a good idea in this patient, but this diagnosis is less likely given her risk factors and findings on chest x-ray.

**28** A 72-year-old man is being hospitalized for pneumonia and suddenly experiences worsened dyspnea. He states that he cannot seem to catch his breath, which is worse than when he first came to the hospital. He has a sharp chest pain that is more painful with deep inspiration. His medical history is significant for diabetes, hypertension, a hemorrhagic stroke with residual left-sided weakness, and chronic hepatitis. He has a temperature of 37.6°C, blood pressure of 138/88 mmHg, heart rate of 134 beats per minute, respiratory rate of 28 breaths per minute, and oxygen saturation of 95%. A Doppler ultrasound study confirms a deep venous thrombosis (DVT) in the lower extremity, and a CT angiogram confirms the diagnosis of pulmonary embolism.

Which of the following should be done next for this patient?

- (A) Start IV enoxaparin
- (B) Place an inferior vena cava (IVC) filter
- (C) Catheter-directed thrombolysis
- (D) Start IV alteplase

**The answer is B: Place an inferior vena cava (IVC) filter.** Even before the CT angiogram confirmed the diagnosis of pulmonary embolism, this diagnosis should have been suggested by the patient's pleuritic chest pain, tachycardia, and tachypnea. (A) The first step in management of an acute pulmonary embolism in a stable patient is anticoagulation; however, this patient has a history of hemorrhagic stroke and therefore anticoagulation is contraindicated. The next step in these patients is to place an IVC filter, which will prevent a second pulmonary embolism that could be lethal. (Interestingly, these filters decrease the risk of future pulmonary emboli, but they have not been shown to decrease overall mortality.) In patients who have a temporary contraindication to anticoagulation and receive an IVC filter, the filter should be removed when they can be anticoagulated safely.

If this patient were hemodynamically unstable, then surgical or catheter-based thrombectomy would be an option. (C) Catheter-directed thrombolysis is an option in patients with extensive DVTs and those that do not meet criteria for surgical thrombectomy. This is an invasive procedure and the patient is hemodynamically stable. (D) Systemic fibrinolytics are used for hemodynamically unstable patients without contraindications, and this patient is stable with an absolute contraindication.

29

A 48-year-old woman comes to the hospital because of difficulty breathing. She also describes some joint pains in her hands and knees, but otherwise has no other complaints. She denies fevers, chest pain, dysuria, or recent illnesses. Her examination is remarkable for dullness to percussion at the base of the right lung, and a chest x-ray confirms the presence of a pleural effusion. A thoracentesis is performed, and the fluid appears turbid. The ratio of pleural fluid protein to serum protein is 0.9, and the glucose is 25 mg/dL (normal >60 mg/dL).

Which of the following is the most likely cause of this patient's pleural effusion?

- (A) Pneumonia
- (B) Nephrotic syndrome
- (C) Rheumatoid arthritis
- (D) Tuberculosis

**The answer is C: Rheumatoid arthritis.** A pleural fluid protein to serum protein ratio >0.5 suggests an exudative effusion. The additional finding of a

**Table 2-2 Hints to the Cause of a Pleural Effusion**

| Clues from Pleural Fluid | Diagnosis                                                                 |
|--------------------------|---------------------------------------------------------------------------|
| Many red blood cells     | Hemothorax, malignancy, pulmonary embolism                                |
| Many lymphocytes         | Tuberculosis, malignancy                                                  |
| Low glucose              | Rheumatoid arthritis, malignancy, infection (empyema), esophageal rupture |
| High amylase             | Pancreatitis, esophageal rupture                                          |
| High triglycerides       | Chylothorax                                                               |

low glucose narrows the differential diagnosis to processes that cause either an increased consumption of glucose within the pleural fluid (by bacteria, neutrophils, malignant cells, etc.), or that disrupt the transport of glucose from the blood to the pleural fluid (e.g., malignancy). These causes include rheumatoid arthritis, parapneumonic effusions or empyemas, tuberculosis, malignancy, and esophageal rupture. The further history of joint pain in the hands and knees suggests the diagnosis of rheumatoid arthritis. **(A, D)** There is not enough information to suggest pneumonia or tuberculosis (no fevers, no suggestion of cough, etc.). **(B)** Nephrotic syndrome causes a transudative effusion. Other clues to the cause of a pleural effusion are summarized in *Table 2-2*.



A 38-year-old woman presents with progressive shortness of breath and a chronic dry cough. Initially, she presented to her primary care provider and had a chest x-ray performed which showed prominent reticular markings in the lung fields. She has no relevant medical history and does not take any medications. She denies any fevers, weight loss, or chest pain. There is a family history of hypertension and dyslipidemia, but no lung or heart disease. She works as a receptionist and has never smoked. On physical examination, there are dry rales throughout both lung fields with scattered wheezes. There is no focal dullness to percussion. Initial laboratory tests are ordered and show a normal hemoglobin and leukocyte count, as well as normal electrolytes and liver enzymes. HIV testing is performed and is negative.

Which of the following should be done next in the workup of this patient?

- (A)** High-resolution computed tomography
- (B)** Chest x-ray
- (C)** Lung tissue biopsy
- (D)** Bronchoscopy

**The answer is A: High-resolution computed tomography.** Diffuse dry rales (crackles) indicate an interstitial lung process such as pulmonary fibrosis. The approach to diagnosing interstitial lung disease starts with taking a good history looking for drug exposures (e.g., methotrexate, bleomycin, amiodarone), radiation exposure, occupational exposures (e.g., asbestosis, silicosis, berylliosis, etc.), and a personal or family history of autoimmune disease. Further workup involves obtaining laboratory values to assess for an underlying disease, but many times the workup is inconclusive. High-resolution CT scans help to make the diagnosis of interstitial lung disease and to differentiate among the various types. Common features of interstitial lung disease are a reticular, nodular, and/or ground glass pattern on imaging. Other features that help to make the diagnosis are the primary location of disease (e.g., bibasilar in rheumatoid arthritis, middle lung fields in connective tissue diseases like scleroderma, and upper lung fields in some occupational exposures such as silicosis), presence of pleural disease (e.g., pleural plaques in asbestosis), lymphadenopathy (e.g., bilateral hilar adenopathy in sarcoidosis), and the presence and location of lung nodules (e.g., centrilobular nodules in hypersensitivity pneumonitis). **(B)** A chest x-ray was recently performed in this patient, and repeating this study is unlikely to yield any new information. **(C)** Biopsy of the lung is a very invasive procedure. It may be performed eventually in this patient, but the next step is further imaging to characterize the lung pathology. **(D)** Bronchoscopy is also an invasive test and would not be helpful as an initial workup.

**31** A 38-year-old woman with no past medical history presents with fatigue, diffuse joint pain, and difficulty breathing upon exertion. The symptoms have developed gradually over the past few months. On review of systems, she also endorses difficulty swallowing and an increased sensitivity to cold temperatures, which make her fingers turn blue. Her vitals show a temperature of 37.3°C, blood pressure of 132/86 mmHg, heart rate of 82 beats per minute, and respiratory rate of 20 breaths per minute. Dry crackles are heard during auscultation primarily over the middle of the lung fields. On skin examination, the patient has skin tightening around the mouth and hands. There are scattered telangiectasias as well as distal calcifications of the fingertips with some ulcerations. An initial workup with laboratory values and imaging is ordered, and pulmonary function testing is performed.

|                           |                   |
|---------------------------|-------------------|
| FEV <sub>1</sub>          | 90% of predicted  |
| FEV <sub>1</sub> /FVC     | 105% of predicted |
| Total lung capacity (TLC) | 72% of predicted  |

What is the most common cause of death in patients with this disease?

- (A) Cardiovascular disease
- (B) Pulmonary disease
- (C) Renal disease
- (D) Infection

**The answer is B: Pulmonary disease.** This patient has systemic sclerosis (scleroderma) and is presenting with findings suggestive of CREST syndrome (Calcinosis, Raynaud phenomenon, Esophageal dysmotility, Sclerodactyly, and Telangiectasias), which is more commonly associated with the limited form of the disease. The diffuse form usually has central skin involvement (upper arms and chest) rather than just acral involvement. Patients with both the limited and the diffuse form have an increased risk of pulmonary fibrosis, which is seen in this patient. Pulmonary function tests will show a restrictive pattern and a loss in total lung volume. The most common cause of death is from pulmonary fibrosis and pulmonary hypertension. (A) Cardiac disease may include pericarditis, myocardial fibrosis, conduction abnormalities, and changes secondary to pulmonary hypertension from lung disease. These findings are less common than lung findings and are not the most common cause of death. (C) Renal disease can present as scleroderma renal crisis, which is acute in onset and rapidly progressive. Before dialysis, this was a major cause of death. (D) Secondary infections of the diseased lungs may occur but is not the most common cause of death.



32 A 59-year-old woman presents with a 2-month history of left shoulder pain and arm weakness. Her past medical history and family history are unremarkable, and she only takes a daily multivitamin. She drinks 2 glasses of wine daily and smokes a pack of cigarettes daily, which she has done since the age of 18. On examination, her vitals are normal. The lungs are clear bilaterally but there is decreased diaphragmatic excursion on the left. On neurologic examination, her right pupil is larger than the left; when a light is shone into the right eye, the pupils become equal in size.

Which of the following is true regarding this condition?

- (A) It involves the C6 and C7 nerve roots
- (B) There may be atrophy and weakness of the intrinsic muscles of the hand
- (C) There may be right-sided facial flushing and impaired perspiration
- (D) It causes vascular congestion of the abdomen and lower extremities

**The answer is B: There may be atrophy and weakness of the intrinsic muscles of the hand.** This patient has Pancoast syndrome, which is caused by an apical tumor in the superior sulcus that causes symptoms based

on the structures on which it impinges. (A) The tumor may involve the C8 and T1 nerve roots, which leads to atrophy and weakness of the intrinsic hand muscles. Tumors in this location can also impinge on the sympathetic chain, causing ipsilateral Horner syndrome. (C) This patient shows signs of Horner syndrome (left-sided ptosis and miosis); loss of sympathetics to the face would also cause ipsilateral (left-sided, not right-sided) anhidrosis and flushing of the face, since the loss of norepinephrine to cutaneous vessels leads to vasodilation. (D) In some cases, the tumor can also compress the superior vena cava (SVC) and cause SVC syndrome, which can manifest with a feeling of facial fullness, distended neck veins, and facial plethora. It would not cause vascular congestion of the abdomen or lower extremities. This patient also has involvement of the phrenic nerve, manifested by decreased diaphragmatic excursion on the left side. For the shelf examination, whenever there is a vignette with a confusing constellation of findings, try to explain them all with one diagnosis; if you do not understand one part of the presentation (such as the phrenic nerve palsy), then focus on the rest of the findings.



A 65-year-old man is brought in to the hospital by his wife because of fatigue and progressive confusion. His laboratory values are shown below.

|                     |             |
|---------------------|-------------|
| Sodium              | 120 mEq/L   |
| Potassium           | 3.8 mEq/L   |
| Blood urea nitrogen | 27 mg/dL    |
| Creatinine          | 0.9 mg/dL   |
| Urine osmolality    | 450 mOsm/kg |

The patient is admitted and given hypertonic saline. A lung mass is subsequently found during chest imaging. This type of cancer is UNLIKELY to cause which of the following physical examination findings?

- (A) Ptosis and anisocoria
- (B) Moon facies, central adiposity, and striae
- (C) Jugular venous distention and dilated superficial veins over the chest
- (D) Symmetric muscle weakness and difficulty arising from a chair

**The answer is A: Ptosis and anisocoria.** Small cell lung cancer commonly causes the syndrome of inappropriate ADH (SIADH), which is seen in this patient with severe hyponatremia as a result of excessive water retention. Ptosis (eyelid droop) with miosis (causing anisocoria, or asymmetry of pupil

sizes) is seen in Horner syndrome, with one cause being non-small cell lung cancer that impinges on the sympathetic chain. **(B, C, D)** These answer choices are more commonly associated with small cell lung cancer than with Horner syndrome. Moon facies, central adiposity, and striae are manifestations of Cushing syndrome, which is caused by ectopic production of ACTH. Vascular congestion is seen in superior vena cava (SVC) syndrome, which is caused by a mass obstructing the SVC that leads to increased venous pressure in the face and upper extremities. Symmetric muscle weakness, especially with initial use (vs. fatigability in myasthenia gravis) suggests Lambert–Eaton syndrome with antibodies directed at presynaptic calcium channels.



A 32-year-old man is brought in by paramedics after being involved in a motor vehicle collision. He has multiple fractures and is hypotensive and tachycardic. Heart sounds are normal, but his neck veins are distended and there are decreased breath sounds on the left side with tracheal shift to the right.

Which of the following should be done immediately?

- (A)** Chest x-ray in the upright position
- (B)** Chest tube placement in the fifth intercostal space along the midaxillary line
- (C)** Needle thoracostomy in the second intercostal space along the midclavicular line
- (D)** Emergency thoracotomy

**The answer is C: Needle thoracostomy in the second intercostal space along the midclavicular line.** This patient has a tension pneumothorax, which may occur after trauma, mechanical ventilation, or in patients with underlying pulmonary disease. The diagnosis is highly suggested by the findings of decreased breath sounds on the affected side, tracheal shift *away* from the affected side, elevated jugular venous pressure, and hypotension. It is caused by a rupture in the visceral pleura that creates a flap, acting as a one-way valve that causes air trapping between the visceral and parietal pleura with each inspiration. This increases the pressure in the intrapleural space, causing collapse of the affected lung and compression of the other lung and the mediastinum. If it progresses, cardiac output will decrease and hypotension will result. If there are findings on history or examination that suggest this diagnosis, immediate decompression with needle thoracostomy should be performed. **(A)** This is an emergency; immediate management is life-saving and should not be delayed for diagnostic confirmation with imaging. **(B)** Chest tube placement should occur after needle thoracostomy, but this takes time to perform and therefore is not the initial step. **(D)** Thoracotomy is a last ditch effort in patient resuscitation and is not a good option here. Indications for emergency thoracotomy include penetrating or blunt trauma with hemodynamic instability despite fluid resuscitation en route to the



Emergency Department. Patients with severe intrathoracic processes such as cardiac tamponade, a large air embolism, or major intrathoracic bleeding from large vessels will benefit most from this procedure.

35

A 33-year-old woman presents with progressive shortness of breath. The symptoms started with exertion, but now she has dyspnea at rest. She has no previous medical problems, no family history of heart or lung disease, and she has never smoked. On examination, she has a holosystolic murmur and an S4, both heard along the left sternal border, and there is jugular venous distention. Her lungs are clear bilaterally with no wheezes or rales. Her lower extremities are nontender and symmetric in size. She is admitted and given supplemental oxygen. A chest x-ray shows mild dilatation of the pulmonary arteries, and the lung parenchyma is normal in appearance.

What is the most likely diagnosis?

- (A) Pulmonary arterial hypertension
- (B) Left heart failure
- (C) Pulmonary embolism
- (D) Chronic obstructive pulmonary disease

**The answer is A: Pulmonary arterial hypertension.** Pulmonary hypertension can be a primary disease process or secondary to other disease processes. Pulmonary arterial hypertension is an idiopathic form of pulmonary hypertension that occurs in the absence of another disease process. It is more common in women, typically manifests around the mid-30's, and has a poor prognosis. If the patient were to undergo right heart catheterization, the right atrial, right ventricular, and pulmonary artery pressures would be elevated with a normal PCWP. The mean pulmonary artery pressure would be >25 mmHg (normal range 9 to 18 mmHg). The clues to the diagnosis include the symptom of progressive dyspnea, evidence of right heart strain/failure (tricuspid regurgitation and right-sided S4), and a chest x-ray showing enlarged pulmonary arteries without any other lung disease.

(B, C, D) These are all causes of secondary pulmonary hypertension. The patient has no rales on lung examination, making left heart failure less likely. She has no clinical evidence of a DVT, and there are no suggested risk factors for her being in a hypercoagulable state, making pulmonary embolism less likely. COPD is also unlikely given that she does not have a smoking history and has no wheezes on examination.

36

A 62-year-old man with a long history of COPD presents for routine follow-up in clinic. His symptoms are well controlled with inhaled albuterol, ipratropium, tiotropium, and fluticasone, and he has had no recent acute exacerbations.

Which of the following findings would be unlikely in this patient?

- (A) Increased pulmonary capillary wedge pressure (PCWP)
- (B) Increased hematocrit
- (C) Increased bicarbonate
- (D) Decreased  $\text{PaO}_2$

**The answer is A: Increased pulmonary capillary wedge pressure (PCWP).** This patient's list of medications indicates that he likely has severe COPD with chronic hypoxemia. PCWP estimates left atrial pressure, which should not be elevated in this patient. One of the feared complications of severe COPD is cor pulmonale, which is the development of right heart failure from pulmonary hypertension caused by lung disease. Pulmonary hypertension is a possibility in this patient with severe disease, and the right-sided pressures (right atrium, right ventricle, pulmonary artery) might be elevated; however, the left atrial pressure (estimated by the PCWP) would be normal. (B) Chronic hypoxemia produces secondary polycythemia. Hypoxemia is sensed by the kidneys, which secrete erythropoietin that acts on hematopoietic stem cells in the bone marrow to increase production of red blood cells. (C) Patients with severe COPD often have chronic hypercapnia (respiratory acidosis) with a compensatory metabolic alkalosis due to increased bicarbonate reabsorption by the kidneys. (D) These patients will have chronic hypoxemia (low  $\text{PaO}_2$ ), and if the value is  $\leq 55$  mmHg, then home oxygen therapy is indicated.

37

A 71-year-old man complains of worsening fatigue and dyspnea on exertion. The symptoms have developed gradually over months to years, and he is now short of breath after walking short distances. He endorses night sweats and a weight loss of 10 kg over the past few months, but denies chest pain or paroxysmal nocturnal dyspnea. He is a retired textile manufacturer and has a 30 pack-year smoking history. On examination, there is some clubbing of the digits. A chest x-ray shows a mild reticulonodular pattern within the lung parenchyma and pleural plaques at the base of the lungs near the diaphragm. Pulmonary function testing shows a normal  $\text{FEV}_1/\text{FVC}$  ratio and reduced total lung capacity.

What is the most common type of cancer associated with this patient's lung disease?

- (A) Bronchogenic carcinoma
- (B) Non-Hodgkin lymphoma
- (C) Small cell lung cancer
- (D) Mesothelioma

**The answer is A: Bronchogenic carcinoma.** This patient has a concerning history for asbestos exposure with the development of lung cancer. Asbestos refers to a group of fibers (serpentine or amphibole) that causes lung

disease years after exposure. Concerning environmental exposures include any careers with exposure to textiles, insulation, shipbuilding, and construction; in addition, exposure to someone with one of these careers is also a risk factor (e.g., wife of a shipbuilder that is exposed to asbestos from her husband's clothing). Asbestos exposure is grouped in the category of pneumoconiosis, which are a collection of diseases caused by inhalation of various inorganic dusts.

The patient has risk factors for asbestos exposure and also has diaphragmatic pleural plaques on chest x-ray, which is virtually pathognomonic for asbestosis. Bronchogenic carcinoma is the most common lung cancer with asbestos exposure, and is dramatically increased with the synergistic effect of smoking. (B) Asbestos exposure also increases the risk of other cancers (laryngeal, biliary, etc.) but non-Hodgkin lymphoma is not one of those cancers. (C) Small cell lung cancer is not the most common type of cancer in these patients. (D) Asbestos is the only known risk factor for mesothelioma, a rare malignant disease of the pleura. However, mesothelioma is not the most common cancer in these patients, especially if there is a strong smoking history that dramatically increases the risk for bronchogenic carcinoma.

38

A 32-year-old man comes to the physician because of sudden onset shortness of breath. He has no medical history and was at rest when the symptoms occurred. He is 193.04 cm (6'4") tall and weighs 74.84 kg (165 lb). There are decreased breath sounds over the right lung field with tracheal deviation to the right. He is admitted and undergoes chest imaging followed by placement of a chest tube. He is imaged again later in the day, which shows a decrease in the intrapleural volume but new fluffy opacities within the right lung.

What is the next step in management?

- (A) Intubation with mechanical ventilation
- (B) Diuresis with loop diuretics
- (C) Broad spectrum antibiotics
- (D) Observation

**The answer is D: Observation.** A complication after a large-volume thoracentesis or re-expansion of a pneumothorax is pulmonary edema, which is termed "re-expansion pulmonary edema." There is debate over the exact mechanism, but some factors include the creation of very negative intrapleural pressures, surfactant dysfunction, and possibly direct injury to the lung during thoracentesis or chest tube placement. Most cases are mild and asymptomatic, and observation is sufficient since it is a self-limited process. In severe cases with hypoxemia, supplemental oxygen and mechanical ventilation are options for management. The other answer choices are unnecessary at this time; (A, B, C) the time course is too short for pneumonia to develop, and both heart failure and ARDS would show bilateral pulmonary edema.

39

A 23-year-old cross country runner with a history of asthma complains of worsening dyspnea and cough during exercise. He currently takes inhaled fluticasone and a long-acting  $\beta$  agonist, with inhaled albuterol used as a rescue medication. He is allergic to aspirin and penicillin. He asks about adding montelukast to his regimen.

What is the mechanism of action of this medication?

- (A) Blocks muscarinic acetylcholine receptors
- (B) Irreversible inhibition of cyclooxygenase-1 and 2
- (C) Blocks the receptor for LTC<sub>4</sub>, LTD<sub>4</sub>, and LTE<sub>4</sub> in the leukotriene pathway
- (D) Inhibition of phospholipase A<sub>2</sub> and disruption of neutrophil endothelial adherence

**The answer is C: Blocks the receptor for LTC<sub>4</sub>, LTD<sub>4</sub>, and LTE<sub>4</sub> in the leukotriene pathway.** Montelukast acts as a leukotriene modifier and is a great therapy for asthma in a subset of patients, especially those with an aspirin allergy or with primarily exercise-induced asthma. (A) This is the mechanism of ipratropium, which can be used in acute asthma exacerbations but is used more commonly in COPD (both for chronic treatment and acute exacerbations). (B) Aspirin irreversibly inhibits COX-1 and COX-2. Both the cyclooxygenase pathway and the leukotriene pathway are part of the eicosanoid pathway, and they diverge from the precursor arachidonic acid. (D) Arachidonic acid is produced from membrane phospholipids via the enzyme phospholipase A<sub>2</sub>, which is inhibited by glucocorticoids. Glucocorticoids also cause lymphocyte destruction and a disruption in the adherence of neutrophils to endothelium, which is why patients that acutely start systemic steroids will have an increased white blood cell count that are predominantly neutrophils.

40

A 54-year-old woman presents with sudden onset shortness of breath. She denies any history of heart or lung disease, but does have a history of hypertension and chronic kidney disease. She takes hormone replacement therapy for menopausal symptoms, smokes cigarettes occasionally, does not drink alcohol, and recently returned from a trip to Hawaii. On examination, the patient is afebrile with a blood pressure of 148/94 mmHg, heart rate of 110 beats per minute, and respiratory rate of 26 breaths per minute. Her pulmonary examination is unremarkable, but she has pain, swelling, and erythema of her right lower extremity.

What is the most appropriate next step in the workup of this patient?

- (A) D-dimers
- (B) Ventilation-perfusion (V/Q) scan
- (C) CT angiogram
- (D) Pulmonary angiography
- (E) Lower-extremity Doppler ultrasound

**The answer is B: Ventilation–perfusion (V/Q) scan.** This patient has a high likelihood of pulmonary embolism based on the following findings: tachycardia, tachypnea, clinical signs of a DVT, recent travel (and thus immobilization), and hormone replacement therapy (causing hypercoagulability). **(D)** The gold standard for the diagnosis of pulmonary embolism was previously pulmonary angiography; however, this procedure carries an unacceptably high morbidity and mortality and therefore is rarely performed. **(C)** CT angiography is the preferred method of diagnosis in patients with a likely diagnosis of pulmonary embolism; however, chronic renal failure is a contraindication to this procedure due to the use of contrast material that can be damaging to the kidneys (contrast-induced nephropathy). In these patients, a V/Q scan is the most appropriate next step and identifies areas of mismatched ventilation and perfusion. Although there is good sensitivity with this procedure, the specificity is poor; however, if there is a high likelihood of pulmonary embolism, the specificity improves dramatically. **(A)** D-dimers have a high sensitivity and are used with a low pretest probability of pulmonary embolism to rule out the diagnosis. A positive test must be followed up with further tests given the low specificity of a positive D-dimers result. **(E)** A Doppler ultrasound of the lower extremities has limited usefulness. If a DVT is diagnosed, then it is treated the same way as pulmonary embolism; however, if there is no DVT on imaging, this does not rule out a pulmonary embolism.

41

A 69-year-old woman presents to her physician complaining of a hoarse voice for the past 3 weeks. She has never had these symptoms before, and cannot identify any alleviating or aggravating factors. She denies any recent respiratory tract infections, difficulty swallowing, or difficulty breathing. Her past medical history is significant for hypertension and diabetes. She has never had any surgeries. She has smoked 2 packs of cigarettes a day for the past 23 years, and does not use any drugs or alcohol. Other than voice hoarseness, her physical examination is unremarkable, including a full neurologic examination. She is referred to an otolaryngologist, who finds that she has left-sided vocal cord paralysis.

Which of the following should be part of the workup of this patient's complaint?

- (A)** Upper esophagogastroduodenoscopy
- (B)** Bronchoscopy
- (C)** CT scan of the chest
- (D)** MRI of the brain

**The answer is C: CT scan of the chest.** This is an older patient with a significant smoking history, raising the suspicion for lung cancer. One of the potential manifestations of lung cancer is a hoarse voice, which occurs due to damage of the ipsilateral recurrent laryngeal nerve. This is a branch of the vagus nerve that innervates all of the intrinsic muscles of the larynx except

the cricothyroid muscle. Because lung cancer is suspected, a CT scan of the chest would be more appropriate than a chest x-ray (since there is a higher pretest probability of lung cancer in this patient and a higher rate of false negatives with chest x-rays). **(A)** Hoarseness can be associated with GERD when it causes irritation of the vocal cords; however, this diagnosis does not fit the patient's history and unilateral nature of the vocal cord paralysis. **(B)** Bronchoscopy would be useful to biopsy the lung cancer if it is present, but it must be localized first with a CT scan. **(D)** The neurologic examination was normal, suggesting that her hoarseness is not related to a cranial nerve palsy. The diagnosis of lung cancer must be made first with a CT before a metastatic workup for staging is completed (which includes an MRI of the brain).

**42** A 32-year-old woman with a history of moderate persistent asthma complains of “white stuff” on her tongue and a feeling of “cotton mouth.” Her asthma is well controlled without any recent exacerbations. Examination shows white plaques adherent to the tongue and buccal mucosa that are removed with scraping.

Which of the following is most likely responsible?

- (A)** Albuterol
- (B)** Fluticasone
- (C)** Prednisone
- (D)** Salmeterol
- (E)** Montelukast
- (F)** Epstein–Barr virus

**The answer is B: Fluticasone.** Inhaled corticosteroids cause local immunosuppression and increase the risk of oral candidiasis. Local treatment is preferable to systemic treatment, and a good option is nystatin swish and swallow. **(A, C, D, E)** Prednisone is the only other medication on this list that would also increase the risk of oral candidiasis; however, this patient has no reason for taking oral steroids (they are given during exacerbations and for severe persistent asthma). Albuterol and salmeterol are short- and long-acting  $\beta_2$  agonists, respectively, and would not cause oral candidiasis. Montelukast is a leukotriene inhibitor with adverse effects of drowsiness, GI complaints, and hypersensitivity reactions. **(F)** Epstein–Barr virus causes oral hairy leukoplakia, which manifests with white plaques that *cannot* be removed with scraping (differentiates it from candidiasis). Unlike oral leukoplakia, which is a precancerous lesion, oral hairy leukoplakia is not precancerous and is fairly specific for HIV infection.

**43** A 56-year-old man with a history of hypertension presents for follow-up after recently increasing his dose of hydrochlorothiazide. He takes no other medications and has no other medical history. There is no family history of hypertension or coronary artery disease, and

he does not smoke or drink alcohol. On review of systems, he reports some mild weight gain and daytime fatigue. On examination, he is afebrile with a blood pressure of 154/96 mmHg, which is similar to his blood pressure at his last visit. His BMI is 36 kg/m<sup>2</sup>.

Which of the following is the most appropriate next step in management?

- (A) Increase the dose of hydrochlorothiazide
- (B) Add lisinopril
- (C) Add levothyroxine
- (D) Polysomnography

**The answer is D: Polysomnography.** Although the vast majority of patients with hypertension have an unknown cause (essential hypertension), there are some secondary causes that are important to remember. Patients with obstructive sleep apnea (OSA) will often complain of loud snoring, daytime sleepiness, and gasping for air or choking during the night. Risk factors for OSA include obesity, male gender, alcohol and tobacco use, and increasing age. It is diagnosed with a sleep study (polysomnography) and treated with continuous positive airway pressure (CPAP) during sleep. Treatment of OSA in this patient will help to reduce his blood pressure.

Other important causes of secondary hypertension include renal artery stenosis (from atherosclerosis or fibromuscular dysplasia), advanced renal disease, hyperaldosteronism, hypercortisolism (Cushing syndrome), pheochromocytoma, and coarctation of the aorta (hypertension in the upper extremities and normo- or hypotension in the lower extremities). It is also important that patients do not take medications that can exacerbate hypertension, such as NSAIDs, OCPs, and steroids. Licorice can also exacerbate hypertension by inhibiting 11 $\beta$ -hydroxysteroid dehydrogenase, which normally degrades cortisol so that it cannot act on mineralocorticoid receptors and increase sodium reabsorption in the distal nephron.

(A) The dose of hydrochlorothiazide has already been increased without any effect. (B) Adding an additional agent such as an ACE inhibitor is a good idea for essential hypertension; however, this patient likely has a secondary cause of hypertension that needs to be addressed first. (C) Though weight gain and fatigue are some of the symptoms of hypothyroidism, it would be inappropriate to start treatment with thyroid hormone replacement before the diagnosis is confirmed with thyroid function tests.

44

A 23-year-old woman is brought into the Emergency Department by her mother for sudden onset of shortness of breath. Her medical history is significant for mental retardation and a DVT of the left lower extremity. She is currently normotensive but tachycardic and tachypneic, and appears very tall with an arm span longer than her body. Examination of the eyes is significant for bilateral lens subluxation inferonasally. The

cardiac and pulmonary examinations are normal. There is swelling of her right lower extremity with pain on dorsiflexion of her right foot.

Which of the following is the best next step in management?

- (A) Check serum D-dimer levels
- (B) Start IV alteplase
- (C) Start IV heparin
- (D) Start oral warfarin

**The answer is C: Start IV heparin.** The patient in this vignette has a history of DVT and clinical signs of a current DVT in her right lower extremity. (Note that Homans sign, which is calf pain with dorsiflexion, is not specific at all.) She is now presenting with shortness of breath, tachypnea, and tachycardia, which is concerning for a pulmonary embolism. Her risk factor for developing clots likely stems from her undiagnosed homocystinuria, which is a genetic disease due to a deficiency in cystathionine  $\beta$  synthase. These patients present with a Marfanoid body habitus, but unlike Marfan syndrome they have mental retardation and a propensity to form clots. Ectopia lentis is seen in both Marfan syndrome and homocystinuria; however, the lens will sublux superotemporally in Marfan syndrome and inferonasally in homocystinuria. Diagnosis of homocystinuria can be made by measuring elevated levels of the amino acid homocysteine in the blood and urine.

When there is a high probability that the diagnosis is pulmonary embolism, then IV anticoagulation may be started during the diagnostic workup. (A) Checking D-dimers is reserved for patients with a low pretest probability of pulmonary embolism, since it is a sensitive but not specific test (and therefore good at *ruling out* disease but not *ruling in* disease). The next diagnostic step should be a CT angiogram. (B) IV alteplase is a recombinant tissue plasminogen activator (tPA) and may be used as a fibrinolytic in hemodynamically unstable patients. This patient is currently stable. (D) IV anticoagulation is preferred to oral anticoagulation, and warfarin is a poor choice since it takes days to weeks to achieve a therapeutic effect. Oral warfarin will likely be started during this patient's hospitalization and taken indefinitely (since she has had multiple DVTs now), but the time to reach its therapeutic effect will need to be bridged with an IV anticoagulant like heparin.

45

A 65-year-old man comes to the Emergency Department with several days of difficulty breathing. His medical history is significant for hypertension, for which he takes propranolol. He has not been to the doctor in years, and reports that he has decreased his level of exercise over the past few years. The patient works in a casino and drinks alcohol moderately. He is afebrile with a respiratory rate of 32 breaths per minute and oxygen saturation of 86% on room air. He has a large chest wall with a decreased diaphragmatic excursion, and there are wheezes and rhonchi heard over both lung fields. An initial arterial blood gas shows a pH of



7.30 and  $\text{PaCO}_2$  of 65 mmHg. He is given supplemental oxygen and some additional laboratory values are drawn, including another arterial blood gas.

|                     |           |
|---------------------|-----------|
| Sodium              | 143 mEq/L |
| Potassium           | 3.9 mEq/L |
| Chloride            | 103 mEq/L |
| Bicarbonate         | 30 mEq/L  |
| Blood urea nitrogen | 28 mg/dL  |
| Creatinine          | 1.2 mg/dL |
| Arterial blood gas  |           |
| pH                  | 7.14      |
| $\text{PaO}_2$      | 95 mmHg   |
| $\text{PaCO}_2$     | 85 mmHg   |

Which of the following is NOT a mechanism responsible for this finding?

- (A) Accumulation of lactate
- (B) Decrease in  $\text{CO}_2$  binding to hemoglobin
- (C) Increased ventilation-perfusion (V/Q) mismatch
- (D) Suppression of hypoxemic respiratory drive

**The answer is A: Accumulation of lactate.** An acute worsening of hypercapnia and respiratory acidosis can be seen when oxygen is administered to patients with COPD who are chronic  $\text{CO}_2$ -retainers. For this reason, when oxygen is administered to these patients the goal is an  $\text{SaO}_2$  of 90% to 94% or a  $\text{PaO}_2$  of 60 to 70 mmHg. **(B, C, D)** There are three reasons why COPD patients can become hypercapnic when excessive oxygen is administered. The primary reason is an increase in V/Q mismatch. Arterioles in the lung are unique compared to the rest of the body in that they vasoconstrict in the presence of hypoxia; with excessive oxygen administration, arterioles in poorly ventilated regions lose this mechanism and vasodilate, leading to increased dead space ventilation and worsened V/Q mismatch. The second mechanism is the Haldane effect, in which an increase in the proportion of oxyhemoglobin decreases the availability of binding sites for  $\text{CO}_2$ . This causes dissociation of  $\text{CO}_2$  from hemoglobin, increasing the concentration of  $\text{CO}_2$  in the plasma. The last mechanism is a decrease in minute ventilation that results from loss of

the hypoxemic respiratory drive signaled by peripheral chemoreceptors. This plays a minor role in the development of hypercapnia in these patients. (A) Lactic acidosis causes an anion gap metabolic acidosis (anion gap  $>12$  mEq/L), which is not the acid–base abnormality in this patient. This patient’s acid–base status represents a chronic respiratory acidosis (from chronic COPD) with a superimposed acute respiratory acidosis due to both the COPD exacerbation and the worsening hypercapnia following oxygen administration. He likely has COPD as a result of his chronic secondhand smoke exposure (casino worker). The patient should also switch antihypertensive medications since nonselective  $\beta$ -blockers cause bronchoconstriction through inhibition of  $\beta_2$  receptors.

46

A 22-year-old woman presents to the hospital with severe dyspnea. She has a history of atopic dermatitis and recently started a topical corticosteroid. She lives with her parents and two younger siblings, one of which recently had an upper respiratory infection. She does not smoke or use any illicit drugs. On examination, her temperature is  $37.8^\circ\text{C}$ , blood pressure is 108/72 mmHg, heart rate is 112 beats per minute, respiratory rate is 26 breaths per minute, and oxygen saturation is 88% on room air. Her systolic blood pressure decreases by more than 10 mmHg during inspiration. She is having difficulty speaking in full sentences and is diaphoretic. There are bilateral inspiratory and expiratory wheezes on examination with no dullness to percussion or tactile fremitus over the lung fields. There is no urticaria or angioedema on skin examination.

Which of the following treatments should be given for this patient’s current condition?

- (A) Cautious oxygen administration, targeting an  $\text{SaO}_2 < 94\%$  to prevent hypercapnia
- (B) IV ceftriaxone and azithromycin
- (C) Subcutaneous epinephrine for bronchodilation
- (D) Nebulized ipratropium for bronchodilation
- (E) Nebulized albuterol for bronchodilation
- (F) Immediate pericardiocentesis

**The answer is E: Nebulized albuterol for bronchodilation.** This patient is suffering an acute asthma exacerbation without a previous asthma diagnosis. She has another component of the atopic triad (eczema), which indicates an increased risk for asthma. She is likely suffering from an asthma exacerbation caused in part by her recent exposure to a viral illness. There were wheezes on examination with no urticaria or angioedema, making an anaphylactic reaction unlikely. Once the reader can guess that the diagnosis is asthma, the next step is knowing how to manage an acute exacerbation.

Management of an acute asthma exacerbation involves oxygen administration as well as intermittent or continuous nebulized albuterol, which is the



## BOX 2-2

## Differences in the Treatment of Acute Asthma and COPD Exacerbations

- Oxygenation: in asthma, the goal  $\text{SaO}_2$  is  $>90\%$ ; in COPD, the goal is 90% to 94% to prevent excessive oxygenation that can lead to hypercapnia and respiratory acidosis
- First-line treatment: in asthma it is albuterol, whereas in COPD it is ipratropium; however, the two are often used together in both diseases if the single agent fails to adequately improve symptoms
- Antibiotics: there is no benefit to routine antibiotics in asthma exacerbations unless there is suspicion for a bacterial infection; there is some benefit to routine antibiotics in COPD

first-line treatment. If the patient fails to respond to albuterol, then ipratropium and magnesium are additional options to promote bronchodilation. Oral corticosteroids should also be given to reduce airway inflammation during and after the exacerbation. Response to therapy can be monitored by following the  $\text{SaO}_2$  as well as either the  $\text{FEV}_1$  or the peak expiratory flow (PEF). Arterial blood gases may also be useful; be concerned about the finding of a normal  $\text{PaCO}_2$ , which is often indicative of respiratory fatigue leading to the requirement of intubation (hypoxemia should cause hyperventilation and hypocapnia). There are important differences between the management of asthma and COPD exacerbations, which is summarized in *Box 2-2*.

(A) Oxygen should be administered to asthmatics with a target  $\text{SaO}_2 >90\%$ . In COPD, the target is 90% to 94% due to the concern for the development of hypercapnia; however, this is not seen in asthma. (B) This patient is unlikely to have pneumonia given that she is afebrile and has no suggestive findings of pneumonia on lung examination. (C) Subcutaneous epinephrine is useful in anaphylaxis, but has no benefit over inhaled  $\beta_2$  agonists in asthma for bronchodilation. (D) Ipratropium is an anticholinergic and is the first-line treatment for COPD exacerbation (although albuterol is often used too); it may be used as an adjunctive therapy in asthma exacerbation, but albuterol is the first-line therapy. (F) Pulsus paradoxus is not specific to cardiac tamponade and can result from airway obstruction, which causes air trapping and hyperinflation of the lungs leading to an increase in intrathoracic pressure and therefore an increase in external pressure around the heart. The rest of the patient's presentation is not consistent with tamponade.



47

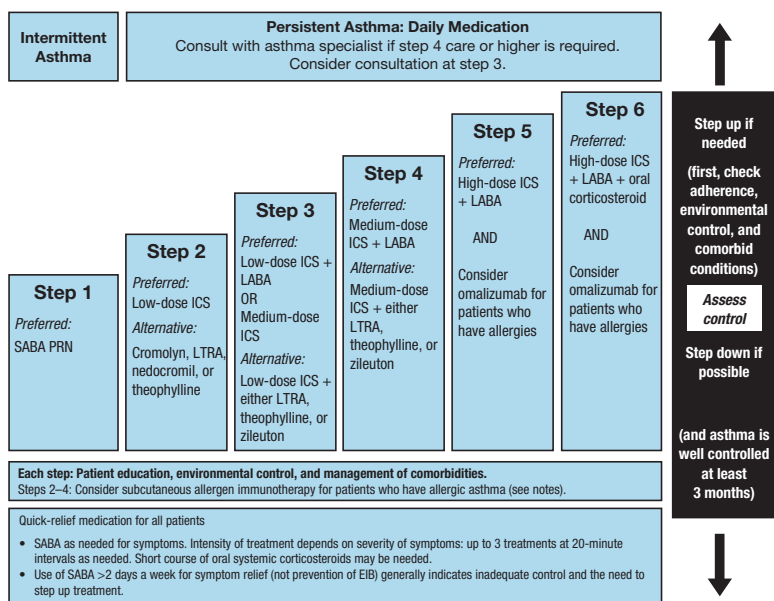
A 28-year-old man with a history of asthma is hospitalized for an acute exacerbation. After discharge, he follows up in clinic. A further history is obtained, and the patient reports daily symptoms with night-time awakenings occurring more than 1 night each week. The symptoms

are especially prominent with exercise. He uses inhaled albuterol as his reliever medication and inhaled fluticasone as his controller medication. Spirometry is performed and shows a mildly reduced FEV<sub>1</sub>/FVC ratio from his baseline.

Which of the following changes to the patient's therapeutic regimen would have been appropriate and might have prevented the acute exacerbation?

- (A) Adding ipratropium
- (B) Adding oral steroids
- (C) Adding salmeterol
- (D) Adding tiotropium
- (E) Adding theophylline
- (F) Adding montelukast
- (G) No change to current regimen

**The answer is C: Adding salmeterol.** Based on his symptoms, this patient's asthma severity can be graded as "moderate." Appropriate management of asthma is somewhat similar to COPD in that there is a stepwise approach to achieve adequate control of the disease. The goal is to have daily symptoms



Key: **Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy.** EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, inhaled long-acting  $\beta_2$ -agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting  $\beta_2$ -agonist

Figure 2-5

2 or less times a week with no nightly symptoms. All patients should be on a reliever medication (rapid acting  $\beta_2$  agonist such as albuterol), but their controller medications can be adjusted based on the severity (*Figure 2-5*). Because this patient requires a step up in therapy, the most appropriate next step would be to add a long acting  $\beta$  agonist (e.g., salmeterol). These medications are especially good for asthma with a strong exercise component. (A, D) Short- and long-acting anticholinergics are more useful in COPD when compared to asthma. (B) Oral steroids are used for acute exacerbations and for chronic severe asthma, using the lowest dose possible; they are not used for chronic therapy in COPD. The patient might be on a steroid taper after his recent acute exacerbation; however, the question is asking about changes to his chronic regimen. (E, F) Theophylline is not a first-line treatment but may be used in patients with difficulty to control asthma. Montelukast and other leukotriene antagonists may be useful as adjunctive therapy. (G) A change in therapy is warranted to achieve symptomatic control.

48

A 21-year-old woman volleyball player complains of chest pain and dyspnea after practice. She finished a vigorous practice and was watching television at home when the symptoms occurred suddenly. She denies any fevers, loss of consciousness, or recent travel. She takes OCPs and her last menstrual period was 2 weeks ago. She does not drink alcohol but admits to smoking cigarettes socially. On examination, she is 183 cm (6'0") tall and weighs 65.77 kg (145 lb). Her blood pressure is 104/68 mmHg, heart rate is 95 beats per minute, and respiratory rate is 28 breaths per minute. There are no murmurs on cardiac examination, and there is no jugular venous distention. There is hyper-resonance to percussion and decreased breath sounds along the right lung field, with normal vesicular sounds along the left lung field. Her trachea is shifted to the right. The rest of the examination is unremarkable.

Which of the following is the most likely cause of this patient's presentation?

- (A) Rupture of an air bleb at the lung apex
- (B) Thromboembolic event in the pulmonary arteries
- (C) Ectopic endometrial glands
- (D) Rupture of the visceral pleura and creation of a one-way valve

**The answer is A: Rupture of an air bleb at the lung apex.** The most common cause of a primary spontaneous pneumothorax is rupture of subpleural blebs (collections of air within the visceral pleura), which commonly occurs while the patient is at rest. These patients will present with symptoms of pleuritic chest pain and shortness of breath, and will have hyper-resonance to percussion with decreased breath sounds in the affected lung due to collapse of that lung. As opposed to a tension pneumothorax,

a spontaneous pneumothorax will draw the unaffected lung and the mediastinum toward the affected lung due to collapse and loss of volume of that lung. This will cause the trachea to shift *toward* the affected lung (whereas in a tension pneumothorax the trachea will shift *away* from the affected lung). Risk factors for spontaneous pneumothoraces include smoking, a family history of pneumothoraces, and Marfan syndrome. Diagnosis can be confirmed with a chest x-ray. Treatment depends on the size of the pneumothorax. For small asymptomatic pneumothoraces, oxygen administration and observation is sufficient. For larger pneumothoraces or if the patient is symptomatic, needle aspiration is appropriate. If they fail this treatment, then a chest tube should be placed. With recurrent pneumothoraces, thoracoscopy should be performed with chemical pleurodesis as an option to prevent recurrence.

(B) This answer choice refers to a pulmonary embolism, which is in the differential diagnosis based on the history but it does not fit with the physical examination findings (the lung examination is commonly normal with a pulmonary embolism). (C) Thoracic endometriosis is a potential cause of spontaneous pneumothorax, but this patient’s last menstrual period was 2 weeks ago and therefore she is close to ovulation in her cycle and not menstruation. (D) A tension pneumothorax will shift the trachea contralaterally and is associated with hypotension and jugular venous distention.

49

A 49-year-old man is hospitalized with fever, shortness of breath, and a productive cough containing rust-colored sputum. On examination, he has dullness to percussion over the right lung base. Thoracentesis is performed with removal of 1.5 L of fluid. The results of laboratory tests and pleural fluid studies are shown below.

|                        |                                         |
|------------------------|-----------------------------------------|
| Glucose                | 120 mg/dL                               |
| Total protein          | 6.8 g/dL                                |
| LDH                    | 75 U/L                                  |
| Pleural fluid studies  |                                         |
| pH                     | 6.90                                    |
| Cell differential      | 7,300/mm <sup>3</sup> (89% neutrophils) |
| Gram stain and culture | pending                                 |
| Total protein          | 6.0 g/dL                                |
| LDH                    | 240 U/L                                 |
| Glucose                | 40 mg/dL                                |

Which of the following is the most appropriate next step in management?

- (A) Observation
- (B) Drainage with a chest tube
- (C) Levofloxacin
- (D) Levofloxacin, gentamicin, and vancomycin
- (E) Video-assisted thoracoscopic surgery (VATS)

**The answer is B: Drainage with a chest tube.** The pleural fluid studies meet Light's criteria for an exudative process, which is likely a parapneumonic effusion (occurring next to a pneumonia) based on the patient's symptoms. The next step is to figure out whether the parapneumonic effusion is complicated or uncomplicated, since this will help to determine the appropriate management. A complicated parapneumonic effusion is defined as a pH <7.2, glucose <60 mg/dL, or a positive Gram stain or culture. If gross pus is removed from the pleural space, then it is likely infected and called an empyema. Uncomplicated effusions typically resolve with antibiotics alone; however, complicated effusions require drainage. The best option for these patients is to drain the effusion with a chest tube.

(A) Observation alone is not appropriate. (C, D) These antibiotic regimens are for inpatient treatment of community-acquired pneumonia and health care associated pneumonia, respectively. Antibiotics should be given, but drainage is also necessary. (E) Chest tube placement (tube thoracostomy) is preferred to more invasive procedures such as VATS. VATS is performed by thoracic surgeons and may be useful if there is a multiloculated empyema that does not drain properly with a chest tube.



A 54-year-old homeless man comes to the Emergency Department complaining of shortness of breath. There is the smell of alcohol on his breath, and obtaining the patient's history is limited. His vitals show a temperature of 37.2°C, blood pressure of 142/90 mmHg, heart rate of 86 beats per minute, respiratory rate of 24 breaths per minute, and oxygen saturation of 94% on room air. For the pulmonary examination, the patient is moved from a supine position to a seated position; however, his dyspnea is exacerbated and he refuses to stay in a seated position. His oxygen saturation also decreases slightly while he is in an upright position. The patient has a distended abdomen with shifting dullness, and there are several spider angiomas over the chest with palmar erythema.

Which of the following is the most likely cause of this patient's chief complaint?

- (A) Hepatopulmonary syndrome
- (B) Congestive heart failure
- (C)  $\alpha_1$ -Antitrypsin deficiency
- (D) Chronic obstructive pulmonary disease
- (E) Polycystic kidney disease

**The answer is A: Hepatopulmonary syndrome.** The presence of dyspnea in a patient with manifestations of chronic liver failure (ascites, spider angiomas, palmar erythema) is suggestive of hepatopulmonary syndrome. The unique features of this disease are the presence of platypnea (worsening dyspnea when moving from a supine to an upright position) and orthodeoxia (decreased  $\text{PaO}_2$  when moving from a supine to upright position). The pathophysiology of this process involves arteriovenous dilatations that are hypothesized to be the result of vasoactive substances (e.g., nitric oxide) not broken down by the failing liver. These dilatations preferentially occur at the lung bases, which creates a V/Q mismatch with hypoxemia and an elevated A-a gradient. When the patient is upright, there is even more perfusion of these dilatations, which worsens the V/Q mismatch and causes further hypoxemia. Diagnosis can be made with a contrast echocardiogram, which can differentiate between intracardiac and intrapulmonary shunts. Treatment involves supplemental oxygen and liver transplantation if the patient is eligible.

The rest of the answer choices would not cause platypnea and orthodeoxia. **(B)** Congestive heart failure presents with orthopnea, which is increased dyspnea when lying flat. When supine, there is increased preload to the failing heart with an increase in pulmonary vascular pressures. **(C)**  $\alpha_1$ -Antitrypsin deficiency is a cause of both lung and liver disease in young patients, though this patient's liver disease is likely related to alcohol abuse. **(D)** COPD can cause a congestive hepatopathy as a late finding in the disease process, which would occur from increased venous pressures as a result of cor pulmonale. **(E)** Polycystic kidney disease is an autosomal dominant disease with the formation of many cysts within the kidneys and potentially the liver as well.

51

A 58-year-old man with no significant medical history presents to the Emergency Department for acute abdominal pain. He is given a diagnosis of acute gastroenteritis and is discharged. Before he leaves, he is told to follow up with his primary care provider because of a small right lung opacity discovered on his chest x-ray. The opacity is 2 cm and completely surrounded by lung parenchyma. The patient is upset because he eats healthy, exercises regularly, has never smoked, and gets an annual physical examination. He denies any fatigue, night sweats, weight loss, cough, or dyspnea, and he reports no previous chest imaging.

Which of the following should be done next in the diagnostic workup?

- (A)** CT scan
- (B)** Biopsy of the lesion
- (C)** Surgical excision
- (D)** Colonoscopy
- (E)** Observation



**The answer is A: CT scan.** This patient is presenting with an incidentally discovered solitary pulmonary nodule (SPN). (E) Most of these nodules are benign (granulomas or hamartomas); however, there is still a significant risk that it is cancerous and thus observation alone is not appropriate. The first step with an SPN is to obtain previous chest imaging to see if it was present before or has grown, and to take a good history looking for lung cancer risk factors (smoking, family history of cancer, etc.). CT of the chest should be performed afterward to better characterize the nodule. The risk of cancer increases based on the size and shape of the nodule, with a spiculated pattern being worrisome. Once all of this information is collected, and the patient is at low risk, he can be followed with serial CT scans for 2 years; if there is no growth over this time, the serial CTs can be discontinued. (B) If the risk is intermediate, then a biopsy should be performed. (C) If the risk is high, then the nodule should be surgically removed. (D) The vignette does not mention when he had his last colonoscopy, but he sees his physician annually and likely received one at the age of 50 and therefore will receive another one at the age of 60. There is no suggestion of metastatic colon cancer in the vignette.

52

A 58-year-old woman presents to the hospital with shortness of breath. There is dullness to percussion at her lung bases, and a thoracentesis is performed. The following results are obtained.

|                          |           |
|--------------------------|-----------|
| Total protein (serum)    | 6.8 g/dL  |
| LDH (serum)              | 75 U/L    |
| Glucose (serum)          | 120 mg/dL |
| Total protein (effusion) | 2.0 g/dL  |
| LDH (effusion)           | 25 U/L    |
| Glucose (effusion)       | 90 mg/dL  |

Based on these findings, which of the following is the most likely underlying diagnosis?

- (A) Nephrotic syndrome
- (B) Rheumatoid arthritis
- (C) Tuberculosis
- (D) Lung cancer

**The answer is A: Nephrotic syndrome.** Any new onset pleural effusion should be “tapped” (thoracentesis) for diagnostic purposes. The first step in determining the etiology is to differentiate between a transudative process and

an exudative process. An exudate is diagnosed when one or more of *Light's criteria* are met: the ratio of total pleural fluid protein to total serum protein is  $>0.5$ , the ratio of total pleural fluid LDH to total serum LDH is  $>0.6$ , or the total pleural fluid LDH is greater than two-thirds the upper limit of normal of serum LDH. Light's criteria is very sensitive but not as specific, so it can misdiagnose a transudate as an exudate (further studies can be performed, which are typically beyond the scope of the shelf examination).

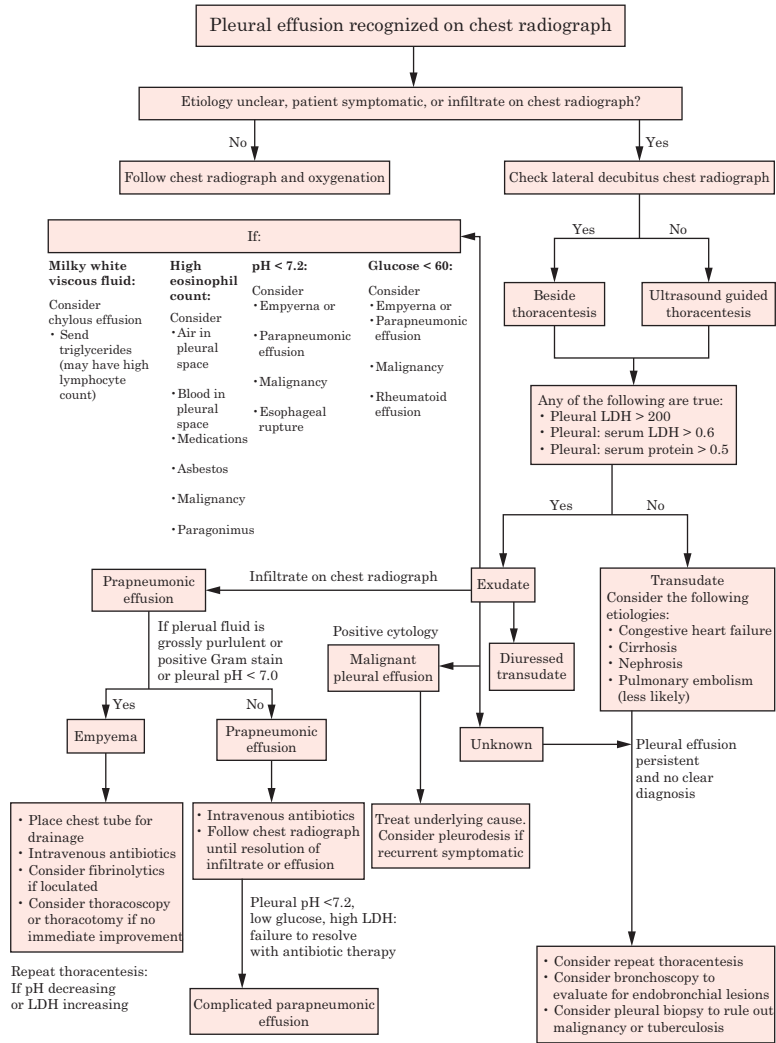


Figure 2-6

Transudates are usually caused by systemic processes resulting in a disruption of hydrostatic or oncotic pressures. Common causes include congestive heart failure, cirrhosis, and nephrotic syndrome. **(B, C, D)** Exudates typically imply local processes and are a result of inflammation causing capillary leak or abnormalities in lymphatic drainage. Rheumatoid arthritis, tuberculosis, and malignancy are all examples of exudative processes. Other examples include any pulmonary infection, pulmonary embolism, systemic lupus erythematosus and other collagen vascular diseases, pancreatitis, hemothorax, and chylothorax. The above is just a partial list, and differentiating the cause of an exudate is much more difficult than a transudate. A useful flowchart for the diagnosis and management of pleural effusions is shown in *Figure 2-6*.

53

A 68-year-old woman presents to the Emergency Department with shortness of breath and right upper quadrant pain. She has a long history of hypertension and COPD, for which she takes captopril and a variety of inhaled medications including ipratropium, albuterol, salmeterol, and fluticasone. Her vitals show a temperature of 37°C, blood pressure of 102/64 mmHg, heart rate of 108 beats per minute, respiratory rate of 30 breaths per minute, and oxygen saturation of 83% on room air. When speaking, she is gasping for air in between words and using accessory muscles of respiration. Her jugular veins are distended, and she has a right ventricular heave with an S4 and a holosystolic murmur at the left lower sternal border. Breath sounds are decreased bilaterally, with scattered wheezes and rhonchi heard over the lung fields without significant rales. In addition, there is hepatomegaly and pitting edema around the ankles. An ECG shows right axis deviation with a right bundle branch block.

Which of the following could have delayed the onset of this complication?

- (A)** Digoxin
- (B)** Diuresis with furosemide
- (C)** Vaccination against pneumococcus and influenza
- (D)** Home oxygen therapy

**The answer is D: Home oxygen therapy.** Cor pulmonale is defined as right ventricular dysfunction as a result of lung disease. COPD is the most common cause of cor pulmonale and causes pulmonary hypertension from emphysematous destruction of the lung parenchyma and vasculature. Chronic pulmonary hypertension will eventually cause right heart failure, which will manifest with jugular venous distention, hepatomegaly, and edema. Important signs of right heart strain from pulmonary hypertension include tricuspid regurgitation, right ventricular heave, S4, and ECG findings of right ventricular hypertrophy. Home oxygen therapy delays the onset

of this deadly complication of COPD by decreasing hypoxemic pulmonary vasoconstriction and therefore decreasing the pressure in the pulmonary artery. This is an important treatment for advanced COPD and has been shown to improve mortality. **(A)** Digoxin is a cardiac glycoside that increases contractility of the ventricles. It is used for symptomatic relief in heart failure; however, it is not very useful in isolated right heart failure and would not delay the development of cor pulmonale in this patient. **(B)** Diuresis is an option for treating heart failure; however, it would not delay the development of cor pulmonale. Diuresis is complicated in patients with cor pulmonale. Some reduction in excessive preload will improve right ventricular cardiac output, but they are also very preload dependent and their cardiac output will decrease quickly if they are diuresed too much. **(C)** Vaccination is an important preventive measure in patients with COPD to reduce the risk of serious lung infections that cause life-threatening acute exacerbations. This patient is afebrile and having shortness of breath as a result of right heart failure, not a respiratory infection.

54

A 28-year-old woman with a history of asthma presents to the Emergency Department complaining of an “asthma attack.” She regularly uses inhaled albuterol and fluticasone, but is experiencing worsening shortness of breath for the past hour and is not responding to the albuterol inhaler. She broke her tibia in a skiing accident 1 week ago and an open reduction with internal fixation was performed. She takes oral contraceptive pills but denies using any other medications. On examination, her heart rate is 115 beats per minute, her respiratory rate is 28 breaths per minute, and her oxygen saturation is 94%. There are no murmurs or abnormal lung sounds. There is a cast on her right lower leg, and the right thigh above the cast is swollen and erythematous compared to the left thigh.

Which of the following is the most likely diagnosis?

- (A)** Pulmonary embolism
- (B)** Fat embolism
- (C)** Acute asthma exacerbation
- (D)** Viral bronchitis

**The answer is A: Pulmonary embolism.** Despite the fact that the patient has asthma and claims to be having an exacerbation, there is no significant wheezing on examination, suggesting an alternative diagnosis. The patient has several risk factors for pulmonary embolism, meeting the three categories of Virchow triad of thrombosis: stasis (likely has some degree of inactivity from her fractured tibia), endothelial injury (fractured tibia and orthopedic surgery), and a hypercoagulable state (oral contraceptive pills). Though the *modified Wells criteria* does not need to be memorized for the examination, it is useful for the discussion of pretest probabilities concerning the diagnosis

of pulmonary embolism. The patient has at least a score of 6 points (3 points for clinical signs of a DVT in the injured leg, 1.5 points for tachycardia, and 1.5 points for recent surgery), although an argument could be made for adding 3 additional points since pulmonary embolism is the most likely diagnosis compared to alternative diagnoses. This gives her a high probability of having a pulmonary embolism (high probability is  $>6$  points, intermediate is 2–6 points, and low is  $<2$  points). Other potential points in the modified Wells criteria include the presence of hemoptysis or malignancy (1 point each) and a history of prior DVTs or pulmonary emboli (1.5 points). A CT angiogram would be the appropriate next step in diagnosis, and she should receive empiric anticoagulation.

**(B)** Fat embolism can occur as a result of a long bone fracture; however, this usually occurs within days of the trauma. Fat emboli syndrome is a distinct entity and presents with dyspnea, neurologic findings, and a petechial rash. **(C)** As mentioned previously, this patient has a history of asthma but you should avoid the temptation to explain her current symptoms with that diagnosis. Always recognize other important historical and physical findings that might fit another diagnosis better. **(D)** Viral bronchitis (like an asthma exacerbation) would present with marked wheezing, which is not seen in this patient.



A 24-year-old man presents with a 1-day history of shortness of breath and hemoptysis. He denies any fever or malaise, and has no significant past medical history. He does not take any medications, smoke, or use illicit drugs; he has not traveled recently or been exposed to any sick contacts. His laboratory values are shown below.

|                     |           |
|---------------------|-----------|
| Hemoglobin          | 11.5 g/dL |
| Sodium              | 143 mEq/L |
| Potassium           | 4.8 mEq/L |
| Chloride            | 111 mEq/L |
| Bicarbonate         | 22 mEq/L  |
| Blood urea nitrogen | 34 mg/dL  |
| Creatinine          | 2.9 mg/dL |

Urinalysis shows 1+ protein with red blood cells and red blood cell casts. There are pulmonary infiltrates on chest x-ray, and a renal biopsy shows linear deposits of IgG along the glomerular capillaries on immunofluorescence.

What other disease process has a similar pathophysiologic mechanism to this patient's disease?

- (A) Pemphigus vulgaris
- (B) Shellfish allergy
- (C) Tuberculin skin test
- (D) Lupus nephritis

**The answer is A: Pemphigus vulgaris.** For patients presenting with pulmonary hemorrhage and renal failure, always consider Goodpasture syndrome and Wegener granulomatosis (now called granulomatosis with polyangiitis). Although lupus and Henoch-Schönlein purpura can cause these findings, it is rare for these diseases to manifest this way and they are less commonly tested. One other important diagnosis to consider is infective endocarditis, since embolic phenomena can affect the lungs and the kidneys; however, for this to happen, both right-sided and left-sided heart valves would have to be infected.

This patient has Goodpasture syndrome, which is suggested by the findings of pulmonary infiltrates on chest x-ray with hemoptysis (pulmonary alveolar hemorrhage) and nephritic syndrome. The diagnosis is confirmed with serum anti-glomerular basement membrane antibodies (anti-GBM) or renal biopsy showing a linear pattern of IgG deposition along the glomerular capillaries. Treatment is with plasma exchange and immunosuppressive medication (prednisone or cyclophosphamide).

The pathophysiology of Goodpasture involves a type II hypersensitivity reaction in which serum antibodies bind to self-antigens ( $\alpha$ -3 chain of type IV collagen, which is found in basement membranes) causing cell death and tissue damage. Pemphigus vulgaris is another type II hypersensitivity reaction in which autoantibodies are directed at desmoglein 1 and/or 3, causing disruption of cell-to-cell adhesion and resulting in skin vesicles, bullae, and erosions. (B) Shellfish allergy is a type I hypersensitivity reaction in which previous sensitization to a shellfish antigen causes development of IgE, which links to mast cells and causes massive histamine release and anaphylaxis upon re-exposure to the antigen. (C) The tuberculin skin test operates via a delayed type IV hypersensitivity reaction, which involves memory T-cells that respond to the antigen and activate macrophages. This process takes approximately 48 hours to occur. (D) Lupus nephritis is a type III hypersensitivity reaction involving immune complex formation, which deposit in tissues and activate the complement cascade and the acute inflammatory response. Because the immune complexes deposit heterogeneously along glomerular capillaries, they will not cause a linear pattern as is seen in Goodpasture's. Remember that type IV hypersensitivity reactions involve T-cells, whereas the other three involve antibodies (IgE in type I and primarily IgG in types II and III).

56

A 55-year-old Caucasian man is brought into the Emergency Department by his wife because of increasing shortness of breath. Symptoms developed gradually over the past few months are exacerbated by exertion, and are associated with a chronic dry cough. The patient's medical history is significant for hypertension and rheumatoid arthritis, and he takes hydrochlorothiazide and daily NSAIDs. He has smoked 2 packs of cigarettes daily for the past 15 years and drinks alcohol moderately. His temperature is 36.7°C, blood pressure is 142/88 mmHg, heart rate is 94 beats per minute, respiratory rate is 24 breaths per minute, and oxygen saturation is 91% on room air. The physical examination is notable for bibasilar dry crackles, a right ventricular heave, clubbing of the digits, and mild pitting edema around the ankles. There is also some tenderness to palpation in the epigastric area. Testing the stool for occult blood is positive.

Which of the following could have prevented the development of this patient's lung disease?

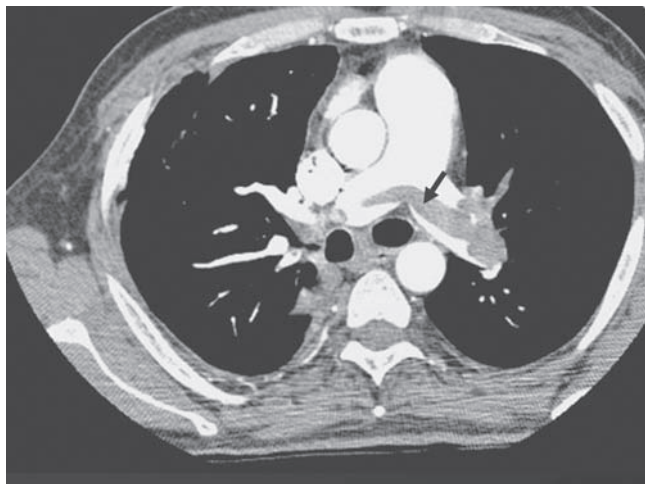
- (A) Adequate blood pressure control
- (B) Smoking cessation
- (C) Early initiation of disease modifying antirheumatic drugs (DMARDs)
- (D) Bronchodilator therapy
- (E) Colonoscopy

**The answer is B: Smoking cessation.** In the setting of rheumatoid arthritis, the symptoms/signs of dyspnea on exertion, chronic dry cough, clubbing, and bibasilar dry crackles are indicative of rheumatoid arthritis-associated interstitial lung disease. This complication typically presents around the age of 50 to 60 and typically affects the lower lungs. Risk factors for developing this complication include male gender, severity of disease (correlates with a high rheumatoid factor level), and smoking. In addition to the presentation, other findings that suggest this diagnosis are a restrictive pattern on pulmonary function tests and reticular or ground glass changes on a CT scan. Smoking cessation is the best preventive measure, and is always a good answer choice for the shelf examination. (C) Early initiation of DMARDs such as methotrexate, azathioprine, rituximab, calcineurin inhibitors, and tumor necrosis factor blockers is a good answer choice since they have been a major improvement in the treatment of patients with rheumatoid arthritis and can slow down disease progression. However, there is less of a correlation between the development of interstitial lung disease and DMARD initiation than other disease features (e.g., joint destruction). Smoking cessation is still the best option for preventing interstitial lung disease associated with rheumatoid arthritis.

(A) Hypertension would not produce the lung findings seen in this patient, and the patient's current blood pressure is only mildly elevated. The findings of a right ventricular heave and peripheral edema may be signs of pulmonary hypertension and early right heart failure (cor pulmonale) from the patient's lung disease. (D) The findings on examination are more consistent with interstitial lung disease (dry crackles) than with COPD (wheezes, hyperinflated lungs). (E) The epigastric pain with occult blood in the stool is likely a result of a bleeding peptic ulcer from chronic NSAID use, not colon cancer. Metastatic disease to the lungs from colon cancer would not produce bibasilar dry crackles.

57

A 68-year-old man undergoes a left hip replacement and is recovering in the hospital afterward. As he stands up to walk with the physical therapist, he suddenly collapses. He undergoes initial resuscitation and is intubated, but he remains hypotensive despite heavy fluid resuscitation. The patient is tachycardic, but the rest of his cardiac and pulmonary examinations are normal. IV heparin is started and a CT angiogram is performed (*Figure 2-7*).



**Figure 2-7**

What is the next step in management?

- (A) Coronary angiography
- (B) Start IV enoxaparin
- (C) Start IV alteplase
- (D) Thrombectomy
- (E) Placement of an inferior vena cava (IVC) filter



**The answer is D: Thrombectomy.** This patient experienced a massive pulmonary embolism, and a “saddle embolus” affecting the pulmonary trunk and arteries is seen on the CT angiogram. Patients undergoing surgical procedures (especially orthopedic surgery) are at an increased risk of clot formation and pulmonary embolism. The initial management of a pulmonary embolism depends on whether the patient is stable or unstable. If the patient is stable and there is a high suspicion for pulmonary embolism, then IV anticoagulation should be started during the workup (e.g., heparin, enoxaparin, fondaparinux, etc.). If a patient has a DVT discovered but is asymptomatic, then the answer is still IV anticoagulation. If the patient is unstable, then they need to be resuscitated and stabilized with ventilation, blood pressure support, and empiric anticoagulation (as long as pulmonary embolism is highly suspected and there are no serious contraindications). (C) Persistent hypotension is an indication for fibrinolytic therapy (alteplase); however, recent surgery within 10 days is a contraindication to this therapy. Other contraindications to fibrinolytics include the presence of an intracranial tumor, recent intracranial surgery or trauma, previous hemorrhagic stroke (or nonhemorrhagic stroke in the past 2 months), internal bleeding within the past 6 months, bleeding diathesis, severe hypertension, and a platelet count  $<100,000/\text{mm}^3$ . Thrombectomy is an option if the patient fails fibrinolytic therapy or has a contraindication to systemic fibrinolysis, and it can be performed surgically or with a catheter. This is the best option for this hemodynamically unstable patient that has a contraindication to fibrinolysis.

(A) The immediate concern is the massive pulmonary embolism on CT, not diagnosing coronary artery disease. (B) Though the patient had recent surgery and therefore is at a higher risk of bleeding, IV anticoagulation is still warranted and the benefits outweigh the risks. Enoxaparin is preferred over heparin by some; however, heparin has already been started and only one agent should be used. (E) An IVC filter is a good option for patients with a confirmed DVT or pulmonary embolism that have a contraindication to anticoagulation (failure of previous anticoagulation, serious bleeding with previous anticoagulation, or high bleeding risk; although recent surgery is a risk factor for bleeding, high risk typically means there are 2 or more risk factors). However, this is not a good option since it will prevent future pulmonary emboli but will not address the current life-threatening embolism!

58

A 57-year-old man is involved in a motor vehicle collision and undergoes operative repair of several fractures. He does well during the procedures and his only complaint is postoperative pain. An arterial blood gas shows a  $\text{PaO}_2$  of 70 mmHg and a  $\text{PaCO}_2$  of 65 mmHg. He has a history of hypertension and stage 2 chronic kidney disease. His regular medications include aspirin and lisinopril. He appears

drowsy on examination but his lungs are clear to auscultation bilaterally.

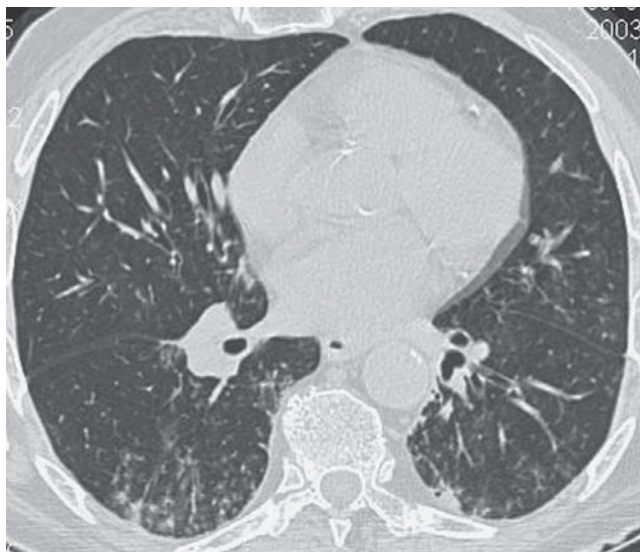
Which of the following is the most likely cause of this patient's abnormal blood gas?

- (A) Medication effect
- (B) Pulmonary embolism
- (C) Postoperative atelectasis
- (D) Hospital-acquired pneumonia

**The answer is A: Medication effect.** Many patients in the hospital are treated with opioids for pain control, which can cause oversedation and hypoventilation. In a patient without pre-existing lung disease, acute hypoxemia with hypercapnia suggests hypoventilation (either a low tidal volume, a low respiratory rate, or both). Besides opioids, other causes of a decreased respiratory rate include sedatives (e.g., benzodiazepines), hypothyroidism, stroke, and metabolic alkalosis. Causes of a decreased tidal volume include obesity, obstructive sleep apnea, COPD, interstitial lung disease, neuromuscular disease (diseases affecting the nerves, neuromuscular junction, or muscles), and chest wall deformities (e.g., severe scoliosis). Diffusion impairment from interstitial lung diseases can also cause hypoxemia and hypercapnia, but not as a result of hypoventilation. (B, C, D) Pulmonary embolism, atelectasis, and hospital-acquired pneumonia cause V/Q mismatch leading to hypoxemia without hypercapnia, since patients will increase ventilation in response to hypoxemia.

59

A 73-year-old nursing home resident complains of severe difficulty breathing. The nursing home staff reports that she has had several episodes of pneumonia since she has been there and is often delirious during the night. She has a history of hypertension, diabetes, dementia, and chronic cough with daily sputum production. Her medications include metformin, hydrochlorothiazide, over-the-counter cough suppressants, and haloperidol as needed. She has a 10 pack-year smoking history and quit 30 years ago. She has a temperature of 38.3°C, blood pressure of 104/62 mmHg, heart rate of 91 beats per minute, respiratory rate of 26 breaths per minute, and oxygen saturation of 94% on room air. The patient's CT scan is shown below (Figure 2-8).



**Figure 2-8**

Which of the following is the most likely cause of this patient's lung findings?

- (A) Smoking history
- (B) Infection with *Pseudomonas*
- (C) Recurrent aspiration events
- (D) Antibodies against type IV collagen

**The answer is C: Recurrent aspiration events.** Bronchiectasis is a destructive process of the airways caused by recurrent infections without the ability to adequately respond to the infections. The inadequate response may be caused by processes such as airway obstruction, immunosuppression, or impaired drainage from the site of infection. Bronchiectasis may present similarly to COPD with a chronic cough, daily sputum production, wheezing, and dyspnea. It is also a common cause of hemoptysis. This patient's CT confirms the diagnosis of bronchiectasis and shows enlarged airways predominantly in the lower lobes, which is likely the result of recurrent aspiration pneumonias (risk factors in this patient are old age and dementia). Other causes of bronchiectasis include cystic fibrosis, obstructions (COPD, lung tumor, mucus plugging), allergic bronchopulmonary aspergillosis, and immunosuppression.

(A) A history of smoking may lead the reader to suspect COPD; however, the CT scan does not fit this diagnosis. In COPD, there is typically bronchial wall thickening from chronic bronchitis and alveolar septal destruction with enlargement of airspaces from emphysema. (B) Recurrent pseudomonal

infections are a *complication* of bronchiectasis, and are unlikely to be the *cause* of bronchiectasis in this patient. Culture of her sputum would likely show mixed flora containing anaerobes since her pneumonia is caused by aspiration events. **(D)** Goodpasture syndrome is an autoimmune disease that affects the lungs and the kidneys and may present with hemoptysis and nephritic syndrome, which are not seen in this patient.



An older man with a history of COPD presents for follow-up after being hospitalized with an acute exacerbation. He asks you what treatments are available to decrease his risk of death.

Which of the following therapies has been shown to reduce long-term mortality in this condition?

- (A)** Guaifenesin
- (B)** Oral prednisone
- (C)** Home oxygen therapy
- (D)** Ipratropium

**The answer is C: Home oxygen therapy.** The two most important interventions for reducing mortality in COPD are smoking cessation and home oxygen therapy, provided that the patient meets certain criteria. Patients with an  $\text{SaO}_2 \leq 88\%$  or  $\text{PaO}_2 \leq 55$  mmHg during rest, exercise, or sleep will benefit from chronic home oxygen therapy with a significant reduction in mortality. The cutoffs are slightly higher in a patient that has polycythemia or cor pulmonale. There are other interventions that show some mortality benefit, but the two interventions mentioned above are the most likely interventions to be tested on the shelf examination. **(A)** Mucolytics such as guaifenesin may partially reduce symptoms from excess airway secretions; however, there is debate over their usefulness and they do not reduce mortality. **(B)** Oral prednisone is used in acute exacerbations to reduce airway inflammation, but chronic treatment with systemic steroids has many side effects and can increase mortality. **(D)** Inhaled ipratropium is useful both in chronic treatment and in acute exacerbations. It decreases symptoms and improves lung function but does not decrease overall mortality.

## Nephrology

1

A 54-year-old man presents to the hospital with a 3-day history of severe nausea, vomiting, and diarrhea. He has been unable to keep down substantial solids or liquids over the past few days and has become progressively weak. He also endorses subjective fevers and occasional abdominal pain. The patient's medical history is significant for hypertension and chronic low back pain, for which he takes lisinopril and ibuprofen. He has a 4-year-old child that he picks up from daycare who has also had diarrhea. On examination, the patient is tachycardic with a blood pressure of 104/84 mmHg. He appears weak with dry mucus membranes. Routine laboratory values are drawn, which show a blood urea nitrogen (BUN) and creatinine of 40 mg/dL and 2.1 mg/dL, respectively. He denies any history of renal disease.

Of the following options, what would be most helpful in determining the etiology of this patient's renal failure?

- (A) Urine dipstick
- (B) Urine sodium
- (C) Fractional excretion of sodium (FENa)
- (D) Renal ultrasound
- (E) No further workup is necessary

**The answer is C: Fractional excretion of sodium (FENa).** Acute kidney injury (AKI) was defined by the Acute Kidney Injury Network (AKIN) as an abrupt rise (within 48 hours) in serum creatinine by  $\geq 0.3$  mg/dL from baseline, a  $\geq 50\%$  increase in serum creatinine from baseline, or oliguria of  $< 0.5$  cc/kg/h for  $> 6$  hours. Once AKI is recognized, the next step in diagnosis is determining whether the etiology is prerenal, intrinsic renal, or postrenal (*Figure 3-1*). These terms reflect the perceived sight of pathology; prerenal AKI is caused by decreased blood flow to the kidneys, intrinsic renal AKI is caused by direct damage to the kidney parenchyma (i.e., to the renal vasculature, tubules/interstitium, or glomeruli), and postrenal AKI is caused by an obstruction in the urinary tract leading away from the kidneys.

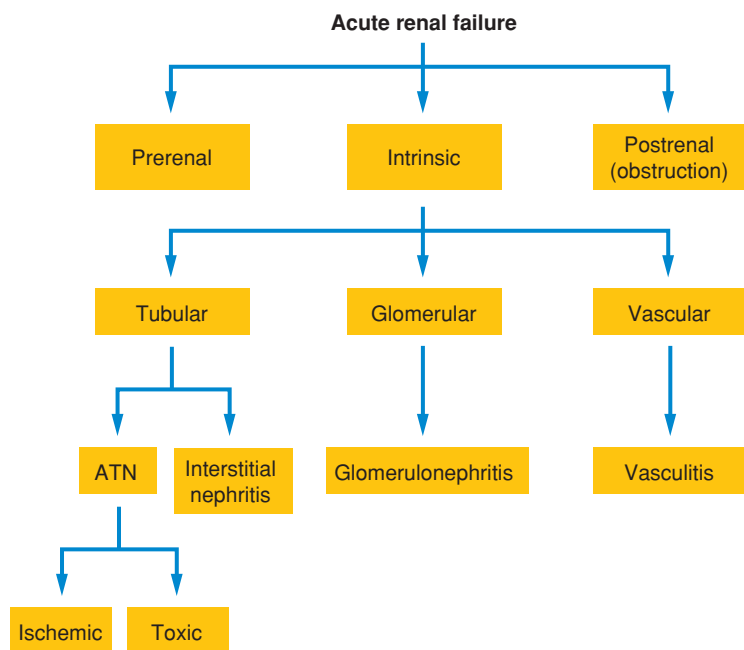


Figure 3-1

The patient in this question is hypovolemic (tachycardia, decreased pulse pressure, and dry mucous membranes) from acute gastroenteritis that he likely acquired from his child. In response to hypovolemia, the renal arterioles vasoconstrict, decreasing blood flow to the kidneys and decreasing the glomerular filtration rate (GFR). Prerenal AKI is a result of ischemia from poor perfusion; however, it can progress to acute tubular necrosis (ATN), which is a form of intrinsic renal AKI. Besides hypovolemia, his daily NSAID may also be contributing to the AKI since NSAIDs cause renal vasoconstriction. The combination of an NSAID and an ACE inhibitor can worsen a more mild renal failure. One of the best tests for differentiating between prerenal AKI and ATN is the FENa. In prerenal AKI, sodium is reabsorbed in an attempt to maintain circulating blood volume, and therefore there will be little sodium in the urine. **(B)** Although this is often reflected by the urine sodium, this value is affected by renal water handling and urine output. FENa is a better test, since it only measures the fraction of sodium excretion and is not affected by urine output. In general, low FENa values indicate prerenal AKI and high values indicate intrinsic renal AKI (tubular damage leads to salt wasting). The FENa will be  $<1\%$  in prerenal AKI and  $>2\%$  in ATN. (Note: FENa should not be used in the setting of diuretics, but the fractional excretion of urea may be used instead.)

(A) A urine dipstick is a helpful screening tool for things like proteinuria or infection, but it will not help to differentiate between prerenal and intrinsic renal AKI. (D) A renal ultrasound is helpful in excluding postrenal AKI, which is not suspected in this case (sudden urinary tract obstruction is unlikely given the patient's history of vomiting and diarrhea). (E) The diagnosis of prerenal AKI versus ATN cannot be made by history alone.



A 68-year-old woman is brought into the Emergency Department because of severe difficulty breathing. She complains that for the past few days she has had a progressive fever and productive cough. She was diagnosed a few weeks ago with idiopathic focal segmental glomerulosclerosis (FSGS), and her other medical problems include hypertension and gastroesophageal reflux disease (GERD). Her vitals show a temperature of 38.3°C, blood pressure of 104/74 mmHg, heart rate of 98 beats per minute, respiratory rate of 22 breaths per minute, and oxygen saturation of 93% on room air. Her laboratory values are shown below.

|                     |           |
|---------------------|-----------|
| Sodium              | 137 mEq/L |
| Potassium           | 4.9 mEq/L |
| Chloride            | 111 mEq/L |
| Bicarbonate         | 16 mEq/L  |
| Blood urea nitrogen | 36 mg/dL  |
| Creatinine          | 1.2 mg/dL |
| Glucose             | 148 mg/dL |
| Albumin             | 2.1 g/dL  |

An arterial blood gas shows a pH of 7.29 and a PaCO<sub>2</sub> of 32 mmHg.

Which of the following is the likely cause of this patient's acid/base status?

- (A) Renal tubular acidosis
- (B) Hyperaldosteronism
- (C) Lactic acidosis
- (D) Excessive IV fluids

**The answer is C: Lactic acidosis.** This patient has sepsis (meets 3/4 systemic inflammatory response syndrome criteria with the likely infectious source being pneumonia) and has an anion gap metabolic acidosis (explained later). The recent diagnosis of nephrotic syndrome put her at an increased risk of infection because

of immunoglobulin loss in the urine. In addition, patients with nephrotic syndrome are also at risk for thrombosis, protein malnutrition, and hypovolemia.

Generally speaking, acid/base problems on the shelf examination will consist of a primary disturbance with a compensatory process (*Table 3-1*); there will likely be no mixed acid/base problems. (Note: a major exception to this is salicylate overdose, in which there will initially be a primary anion gap

**Table 3-1 Overview of Acid/Base Problems**

| Disturbance                     | Laboratory Findings                               | Compensation                                                                                                                                  | Differential Diagnosis                                                                                                                                                                         |
|---------------------------------|---------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Anion gap metabolic acidosis    | ↓ pH, ↓ HCO <sub>3</sub> ,<br>↓ PaCO <sub>2</sub> | Respiratory alkalosis<br>• Winter formula:<br>$\text{PaCO}_2 = (1.5 \times \text{HCO}_3) + 8 \pm 2$                                           | <i>MUDPILES</i> : Methanol, Uremia, Diabetic (or alcohol/starvation) ketoacidosis, Paraldehyde (or Propylene glycol), Isoniazid, Lactic acidosis, Ethylene glycol, Rhabdomyolysis, Salicylates |
| Nonanion gap metabolic acidosis | ↓ pH, ↓ HCO <sub>3</sub> ,<br>↓ PaCO <sub>2</sub> | Same as above                                                                                                                                 | <i>HARDUP</i> : Hyperalimentation (e.g., TPN), Acetazolamide, Renal tubular acidosis, Diarrhea, Ureteral diversion, Pancreatic fistula                                                         |
| Metabolic alkalosis             | ↑ pH, ↑ HCO <sub>3</sub> ,<br>↑ PaCO <sub>2</sub> | Respiratory acidosis<br>• ↑ 7 PaCO <sub>2</sub> per ↑ 10 HCO <sub>3</sub>                                                                     | Vomiting, diuretics, hyperaldosteronism, hypovolemia (contraction alkalosis), hypokalemia                                                                                                      |
| Respiratory acidosis            | ↓ pH, ↑ HCO <sub>3</sub> ,<br>↑ PaCO <sub>2</sub> | Metabolic alkalosis<br>• Acute: ↑ 1 HCO <sub>3</sub> per ↑ 10 PaCO <sub>2</sub><br>• Chronic: ↑ 4 HCO <sub>3</sub> per ↑ 10 PaCO <sub>2</sub> | Pulmonary disease, neuromuscular disease, chest wall deformities, CNS depression (sedatives, trauma, etc.)                                                                                     |
| Respiratory alkalosis           | ↑ pH, ↓ HCO <sub>3</sub> ,<br>↓ PaCO <sub>2</sub> | Metabolic acidosis<br>• Acute: ↓ 2 HCO <sub>3</sub> per ↓ 10 PaCO <sub>2</sub><br>• Chronic: ↓ 4 HCO <sub>3</sub> per ↓ 10 PaCO <sub>2</sub>  | Hypoxemia and primary hyperventilation (CNS disease, salicylate intoxication, pregnancy, anxiety)                                                                                              |



metabolic acidosis with a primary respiratory alkalosis.) The first step in any acid–base problem is determining if there is an anion gap using the equation:  $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$ . If so, then there is at least one type of metabolic acidosis (one can determine if there is another metabolic acidosis by checking the delta–delta, but this is probably beyond the scope of the examination). Next, check the pH, bicarbonate, and  $\text{PaCO}_2$  to determine the primary acid/base disorder. This will open up a list of potential differential diagnoses, only one of which will fit the findings in the vignette.

An important part of this question is recognizing the anion gap metabolic acidosis. The initial calculated anion gap is 10 (normal range 6 to 12); however, this needs to be corrected for the low albumin. For every drop in albumin by 1, the *expected* anion gap drops by 2.5. The corrected anion gap is therefore 15, so there is an anion gap metabolic acidosis. Because this patient is septic, she likely has lactic acidosis. (She likely has a mixed acid/base picture with a primary respiratory alkalosis as a result of hypoxemia from pneumonia, but this is not important for the question.) **(A, D)** Both renal tubular acidosis and excessive IV saline administration will cause a nonanion gap metabolic acidosis. **(B)** Hyperaldosteronism will cause a metabolic alkalosis.



A 43-year-old Caucasian man comes to the physician because of fatigue and body swelling that has developed over the last few weeks. He has no significant medical history, and takes no medications. He does not smoke or drink alcohol, and exercises 3 times weekly. He is afebrile with a blood pressure of 128/86 mmHg, heart rate of 88 beats per minute, and respiratory rate of 16 breaths per minute. On physical examination, there is noticeable periorbital edema with diffuse edema of the extremities. His laboratory values are shown below.

|                     |            |
|---------------------|------------|
| Sodium              | 138 mEq/L  |
| Potassium           | 4.5 mEq/L  |
| Chloride            | 104 mEq/L  |
| Bicarbonate         | 24 mEq/L   |
| Blood urea nitrogen | 8 mg/dL    |
| Creatinine          | 0.9 mg/dL  |
| Glucose             | 146 mg/dL  |
| Albumin             | 2.8 g/dL   |
| Urine dipstick      | 3+ protein |

Which of the following is also likely to be present in this patient?

- (A) HIV infection
- (B) Hypercholesterolemia
- (C) S3 on cardiac auscultation
- (D) Hematuria

**The answer is B: Hypercholesterolemia.** This patient has three characteristics of nephrotic syndrome: proteinuria, hypoalbuminemia, and generalized edema. Nephrotic range proteinuria must be confirmed with a 24-hour urine sample and is defined as  $>3.5$  g/d. Another important characteristic of nephrotic syndrome is hyperlipidemia. In response to the reduction in plasma oncotic pressure due to the loss of albumin and other plasma proteins in the urine, the liver increases synthesis of lipoproteins resulting in hypercholesterolemia. In addition, there is impaired liver metabolism that often results in hypertriglyceridemia. Finally, lipiduria may also be present and is manifested as urine fatty casts with a “Maltese cross” appearance.

(A) FSGS is the most common glomerulopathy in the setting of HIV infection. However, this patient does not have apparent risk factors for HIV infection and he better fits the epidemiologic profile of membranous nephropathy (middle-aged Caucasian). FSGS is seen more commonly in African American and Hispanic patients. (C) This patient has characteristics of nephrotic syndrome and therefore heart failure is not the correct diagnosis. (D) Though there is some overlap of nephrotic and nephritic syndromes, as well as the causes of each, hematuria is typically a feature of nephritic syndrome. There are typically few or no cells in the urine of nephrotic patients.

4

A 58-year-old man with congestive heart failure (CHF), hypertension, and dyslipidemia presents to his physician with low back pain. He complains that he was lifting a heavy box 1 week ago and felt sudden pain in his lower back. He denies any incontinence, lower-extremity weakness, or paresthesia. He has been taking acetaminophen and naproxen around the clock with little effect. His chronic medications include aspirin, carvedilol, furosemide, losartan, simvastatin, and niacin. There is some tenderness to palpation of the paraspinal muscles along the lower back, but the rest of the musculoskeletal and neurologic examinations are normal. Laboratory values are significant for a potassium of 5.2 mEq/L, a BUN of 42 mg/dL, and a creatinine of 1.9 mg/dL (baseline 1.2 mg/dL). A urinalysis is unremarkable except for few hyaline casts.

Which of the following best represents the physiologic changes in the kidney that led to this patient's acute kidney injury? (Note: GFR is glomerular filtration rate, IGP is intraglomerular pressure, AAT is afferent arteriole tension, and EAT is efferent arteriole tension.)

|     | Glomerular Filtration Rate | Intraglomerular Pressure | Afferent Arteriole Tension | Efferent Arteriole Tension |
|-----|----------------------------|--------------------------|----------------------------|----------------------------|
| (A) | ↓                          | ↑                        | ↓                          | ↓                          |
| (B) | ↓                          | ↓                        | ↑                          | ↓                          |
| (C) | ↓                          | ↓                        | ↓                          | ↓                          |
| (D) | ↑                          | ↑                        | ↓                          | ↑                          |
| (E) | ↓                          | ↓                        | ↓                          | ↑                          |

**The answer is B: Decreased GFR, Decreased IGP, Increased AAT, Decreased EAT.** This patient has prerenal AKI as indicated by the abrupt rise in creatinine, the BUN to creatinine ratio  $>20$ , and a bland urinalysis with few hyaline casts (nonspecific, but can be found in prerenal AKI). It is important to recognize risk factors for AKI, and this patient has a few. He has a baseline decrease in effective circulating volume due to heart failure, which causes two important results. The first is an increase in sympathetic activity and therefore an increase in systemic vascular resistance. An increase in norepinephrine causes afferent arteriole vasoconstriction, decreasing the GFR. The second important result of decreased effective circulating volume is activation of the renin–angiotensin–aldosterone system (RAAS, *Figure 3-2*) by the kidneys in response to decreased blood flow. Angiotensin II causes efferent arteriole vasoconstriction, increasing the GFR. Overall, the net effect of decreased effective circulating volume is a decrease in GFR, which will continue to decline as activation of the RAAS leads to salt and water retention that worsens the patient's already reduced cardiac function. However, the patient is on appropriate medications to counteract some of these harmful responses: diuretics, a  $\beta$ -blocker, and an angiotensin receptor blocker (ARB).

Another important consideration in this case is the patient's use of both an ARB and an NSAID. ARBs will block the effect of angiotensin II on the efferent arteriole, thus causing relaxation of the efferent arteriole (decreasing IGP and GFR). The kidneys produce prostaglandins (primarily prostaglandins E<sub>2</sub> and I<sub>2</sub>) that cause afferent arteriole vasodilation to preserve renal blood flow, and prostaglandin synthesis is elevated in situations of decreased effective circulating volume. By blocking the cyclooxygenase (COX) enzymes, NSAIDs inhibit the production of these prostaglandins, which leads to afferent arteriole vasoconstriction (decreasing GFR). It is important to remember that the combination of ACE inhibitors or ARBs with NSAIDs can lead to prerenal AKI or ischemia-induced ATN.

(Note: Ang-I is angiotensin I, Ang-II is angiotensin II, CO is cardiac output, and MAP is mean arterial pressure.)

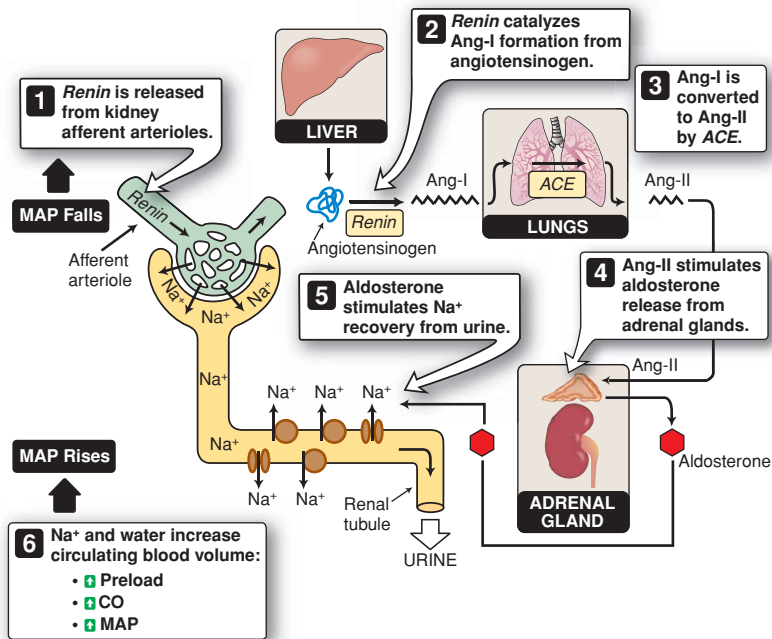


Figure 3-2

**5** A 68-year-old man presents to the hospital with nausea, vomiting, muscle weakness, and palpitations. He has a history of ischemic cardiomyopathy and takes lisinopril, carvedilol, simvastatin, and aspirin. He recently started taking spironolactone due to an increase in heart failure symptoms. There are no recent changes in his diet, and he denies any chest pain or shortness of breath. His screening chemistry panel is shown below.

|                     |           |
|---------------------|-----------|
| Sodium              | 135 mEq/L |
| Potassium           | 7.0 mEq/L |
| Chloride            | 101 mEq/L |
| Bicarbonate         | 24 mEq/L  |
| Blood urea nitrogen | 18 mg/dL  |
| Creatinine          | 1.2 mg/dL |
| Glucose             | 145 mg/dL |

Which of the following treatments is LEAST beneficial in the acute setting?

- (A) Insulin
- (B) Calcium gluconate
- (C) Sodium polystyrene sulfonate
- (D) Furosemide

**The answer is C: Sodium polystyrene sulfonate.** This patient presents with symptoms and laboratory confirmation of hyperkalemia, which is likely caused by the recent addition of spironolactone to his medication regimen. Spironolactone inhibits aldosterone's actions on the distal convoluted tubule of the nephron, which normally upregulates apical sodium channels and increases the activity of the sodium-potassium ATPase. The potential consequence is a rise in serum potassium concentration. ACE inhibitors have the effect of reducing the production of aldosterone, and therefore have a similar effect.

Sodium polystyrene sulfonate (kayexalate) is a cation exchange resin that increases potassium excretion in the GI tract and effectively removes potassium from the body; however, it takes hours to work and is the least beneficial in the acute setting. (B) The most rapid acting treatment of hyperkalemia is calcium gluconate, which acts within minutes to transiently stabilize cardiac membranes in order to prevent the fatal arrhythmogenic complications of hyperkalemia. (A) Insulin is used for its effect of increasing the activity of the sodium-potassium ATPase, driving potassium into cells. It should be given with sugar to prevent hypoglycemia. It is important to note that both calcium and insulin are important in the acute treatment but do not reduce total body potassium; they are "temporizing" measures. Sodium polystyrene sulfonate, furosemide, and hemodialysis are the only options that will reduce total body potassium. (D) Furosemide is a loop diuretic that causes potassium excretion in the urine, and takes roughly 30 minutes to work. Other options for the treatment of hyperkalemia include  $\beta_2$  agonists (e.g., albuterol) and bicarbonate.



A 21-year-old college student presents to the Emergency Department with severe epigastric abdominal pain that radiates to her back. She is nauseous but has not vomited, and denies any diarrhea. She is admitted and her laboratory values show an elevated serum amylase and lipase.

Which of the following electrolyte abnormalities is associated with this disease?

- (A) Hypernatremia
- (B) Hyponatremia
- (C) Hyperkalemia
- (D) Hypokalemia
- (E) Hypercalcemia
- (F) Hypocalcemia
- (G) Hypermagnesemia
- (H) Hypomagnesemia

**The answer is F: Hypocalcemia.** The first step is making the diagnosis of acute pancreatitis, which in her case is likely from alcohol. Acute pancreatitis can cause hypocalcemia due to extravascular binding of calcium to free fatty acids, which surround the pancreas as a result of pancreatic autodigestion by lipase. The other electrolyte abnormalities are not as strongly associated with acute pancreatitis as hypocalcemia.

Note: One important teaching point for the interpretation of serum calcium is that the total calcium level represents both the ionized form (the physiologically active form) as well as the 45% that is bound to serum proteins (primarily albumin). Therefore, patients with low albumin will have a low total calcium but a normal ionized calcium level and will likely not have any symptoms. On the other hand, alkalosis will increase the binding affinity of albumin for calcium, causing a low ionized calcium but a normal total calcium. Bottom line: Do not be tricked by a “low” total calcium level in the setting of low albumin; you must correct for the low albumin.

7

A 52-year-old man presents for a routine physical examination. He has not been to a primary care physician since he was a teenager, and now he wants a colonoscopy since his friend was recently diagnosed with colon cancer. He denies any medical history and takes no medications. He is found to be hypertensive during his clinic appointment (164/98 mmHg), and the diagnosis of hypertension is later confirmed with the use of outpatient blood pressure monitoring. On examination, a bruit is heard over the left carotid artery, an S4 is heard on cardiac auscultation, and he has weak lower-extremity pulses. He has baseline laboratory tests drawn, is started on lisinopril, and is instructed to follow up for repeat laboratory work 1 week later. At the follow-up appointment, his blood pressure is 172/102 mmHg and the following laboratory results are seen.

|                     | First Visit            | Second Visit        |
|---------------------|------------------------|---------------------|
| Sodium              | 142 mEq/L              | 137 mEq/L           |
| Potassium           | 3.2 mEq/L              | 4.3 mEq/L           |
| Chloride            | 105 mEq/L              | 103 mEq/L           |
| Bicarbonate         | 27 mEq/L               | 23 mEq/L            |
| Blood urea nitrogen | 14 mg/dL               | 24 mEq/L            |
| Creatinine          | 1.1 mg/dL              | 1.8 mg/dL           |
| Glucose             | 154 mg/dL (nonfasting) | 120 mg/dL (fasting) |

What should be done next in the management of this patient?

- (A) Add hydrochlorothiazide
- (B) Add metformin
- (C) Stop lisinopril
- (D) Continue the current management and repeat laboratory tests in 2 weeks

**The answer is C: Stop lisinopril.** This patient has an abrupt rise in creatinine after 1 week of taking an ACE inhibitor, indicating that this medication may have caused acute renal failure. One potential side effect of ACE inhibitors and ARBs is a reduction in GFR, which occurs within several days after starting therapy. Although it is rare for these medications to cause AKI, patients with the following conditions are at risk: chronic kidney disease (CKD), polycystic kidney disease, heart failure, hypertensive nephrosclerosis, and bilateral renal artery stenosis.

This patient has hypertension with physical examination findings that suggest chronic hypertension (S4) and peripheral arterial disease (carotid bruit, weak peripheral pulses). In addition, he has hypokalemia at baseline. One condition that should be considered is bilateral renal artery stenosis from atherosclerosis. Because patients with this condition have poor kidney perfusion at baseline, they are in a high renin, high aldosterone state (potentially causing hypokalemia) with dilation of the afferent arteriole and vasoconstriction of the efferent arteriole to maintain GFR. ACE inhibitors cause relaxation of the efferent arteriole through a reduction in angiotensin II, further decreasing GFR and potentially causing ischemic AKI. Other clues to the diagnosis of renal artery stenosis are a renal bruit on examination and episodes of flash pulmonary edema. Bilateral renal artery stenosis can also be caused by fibromuscular dysplasia, which is less common and typically occurs in young women.

(A) The first step in the treatment of AKI is to remove the offending agent, so treating his hypertension and ignoring his AKI is not the right answer. (B) The patient is prediabetic and should be encouraged to change his diet and lifestyle before pursuing pharmacotherapy. (D) It is not appropriate to continue therapy with an agent that precipitated AKI.



A 38-year-old woman presents to her physician with fatigue and edema. She is an IV drug abuser and has been diagnosed with chronic hepatitis C infection. A urinalysis shows 1+ protein, 1+ blood, and red blood cell (RBC) casts. The rest of her laboratory values are shown below.

|                     |                                      |
|---------------------|--------------------------------------|
| Blood urea nitrogen | 25 mg/dL                             |
| Creatinine          | 1.7 mg/dL                            |
| Total protein       | 6.1 g/dL                             |
| Albumin             | 3.7 g/dL                             |
| C3                  | 68 mg/dL (normal range 75–175 mg/dL) |
| C4                  | <2 mg/dL (normal range 14–40 mg/dL)  |

Laboratory testing 2 weeks ago showed a normal creatinine (0.8 mg/dL). A renal biopsy is performed which shows glomerular crescent formation. Antinuclear antibody, antinuclear cytoplasmic antibody, and antiglomerular basement membrane (GBM) antibody testing is negative.

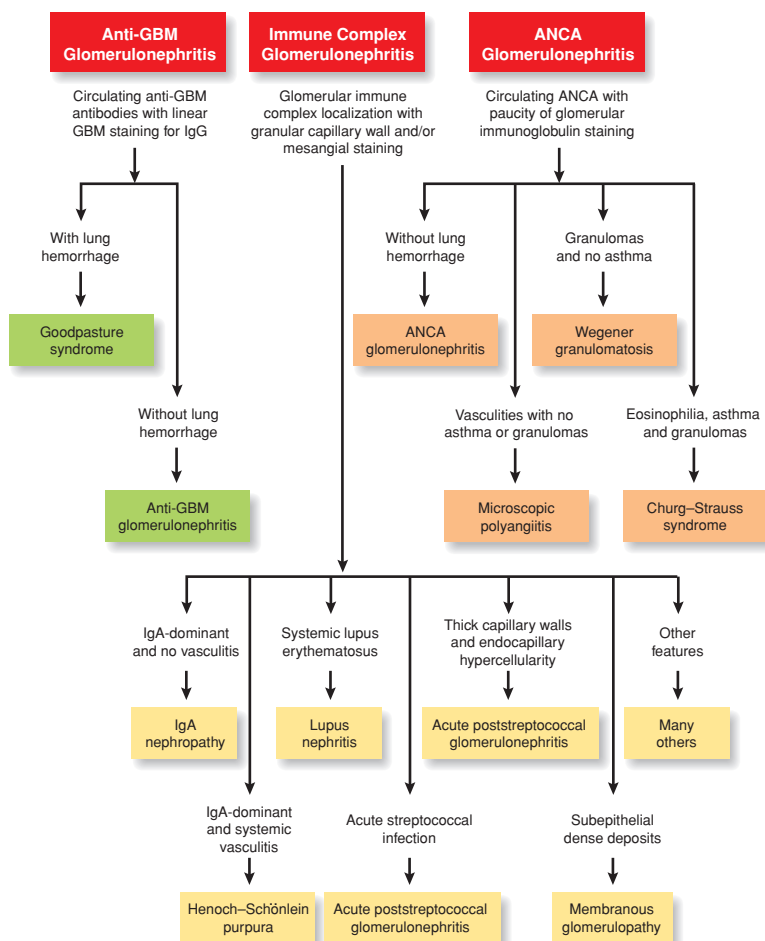
Which of the following is the most likely diagnosis?

- (A) Granulomatosis with polyangiitis
- (B) Systemic lupus erythematosus (SLE)
- (C) Membranoproliferative glomerulonephritis
- (D) IgA nephropathy
- (E) Goodpasture syndrome

**The answer is C: Membranoproliferative glomerulonephritis.** This patient has a rapidly progressive glomerulonephritis (RPGN) indicated by three things: the rapid decrease in GFR over a short period of time, RBC casts on urinalysis that suggests a glomerulonephritis, and crescent formation on renal biopsy. (A) The most common causes of RPGN are antineutrophil cytoplasmic antibody (ANCA)-positive vasculitides (e.g., granulomatosis with polyangiitis); however, testing for ANCA was negative in this case. (E) Goodpasture syndrome can also cause RPGN, but was ruled out with negative anti-GBM antibodies. Therefore, the cause of this patient's RPGN is likely immune-complex mediated, and the next step in diagnosis is looking at serum complement levels. (D) This patient had low complement levels, ruling out causes of



RPGN with normal complement levels such as IgA nephropathy and Henoch–Schönlein purpura. **(B)** SLE can cause RPGN with low complement levels; however, antinuclear antibody (ANA) is a sensitive test and therefore rules this out. Membranoproliferative glomerulonephritis may or may not be associated with cryoglobulins and has a variety of causes, including infections (e.g., HIV, hepatitis C, hepatitis B), collagen vascular diseases (e.g., SLE, rheumatoid arthritis), and monoclonal gammopathies (e.g., multiple myeloma). This patient has chronic hepatitis C infection and this is likely the cause. Below is a helpful overview of the various causes of glomerulonephritis (*Figure 3-3*).



**Figure 3-3**

9

A 69-year-old man presents to the physician for fatigue and bone pain. His workup shows that he is anemic with the presence of an M-protein in the serum and urine, and he is diagnosed with multiple myeloma. Some of his other laboratory values are shown below.

|             |           |
|-------------|-----------|
| Sodium      | 140 mEq/L |
| Potassium   | 3.2 mEq/L |
| Chloride    | 114 mEq/L |
| Bicarbonate | 16 mEq/L  |
| Phosphorus  | 1.9 mg/dL |

An arterial blood gas shows that he has a pH of 7.3 and a  $\text{PaCO}_2$  of 35 mmHg. He has urine studies performed, which are significant for glucosuria, a urine pH of 7.8 after bicarbonate infusion, and a fractional excretion of bicarbonate of 25%.

Which of the following best represents the acid/base abnormality in this patient?

- (A) Anion gap metabolic acidosis with a compensatory respiratory alkalosis
- (B) Nonanion gap metabolic acidosis with a compensatory respiratory alkalosis
- (C) Anion gap metabolic acidosis with a primary respiratory acidosis
- (D) Nonanion gap metabolic acidosis with a primary respiratory acidosis

**The answer is B: Nonanion gap metabolic acidosis with a compensatory respiratory alkalosis.** This question is a good reminder to read the question and skim the answer choices first before going on to read the vignette. In this case, the diagnosis of multiple myeloma and proximal (type 2) renal tubular acidosis (presenting with the Fanconi syndrome, which is a syndrome of proximal tubule dysfunction with a decrease in the reabsorption of bicarbonate, phosphate, amino acids, and glucose) are not important for answering the question, which happens often on the shelf examination. (A, C) From the laboratory values, the calculated anion gap is 10, ruling out an anion gap metabolic acidosis. The pH, bicarbonate, and  $\text{PaCO}_2$  are all low, indicating a metabolic acidosis. To compensate, patients will increase their ventilation to decrease the amount of  $\text{CO}_2$  in the blood, producing a compensatory respiratory alkalosis. To determine if the respiratory compensation is appropriate, Winter formula can be used:  $\text{PaCO}_2 = (1.5 \times \text{HCO}_3) + 8 \pm 2$ . (D) In the case above, the  $\text{PaCO}_2$  should be 30 to 36 mmHg, which fits with the actual value of

35 mmHg confirming that the compensation is appropriate. If the patient were overcompensating (e.g.,  $\text{PaCO}_2$  28 mmHg), then a primary respiratory alkalosis would be present; if undercompensating (e.g.,  $\text{PaCO}_2$  38 mmHg), then a primary respiratory acidosis would be present.

Briefly, monoclonal gammopathies are the most common cause of acquired type 2 renal tubular acidosis, which is caused by an inability of the proximal convoluted tubule to reabsorb important compounds (e.g., bicarbonate, glucose, phosphate, etc.). Patients will excrete bicarbonate in the urine, leading to a moderate nonanion gap metabolic acidosis. The diagnosis is confirmed by an inappropriately elevated urine pH in response to a bicarbonate infusion as well as an increased fractional excretion of bicarbonate  $>15\%$ . Distal (type 1) renal tubular acidosis is caused by a failure to reabsorb bicarbonate in the distal convoluted tubule, leading to severe acidosis with a urine pH consistently  $>5.3$ . Type 4 renal tubular acidosis is a result of hypoaldosteronism and will produce a mild acidosis.



**10** A patient with end-stage renal disease caused by diabetic nephropathy is scheduled to start dialysis due to fluid overload and electrolyte abnormalities.

Which of the following best represents the likely changes seen in her laboratory results? (Note: Hb is hemoglobin, PTH is parathyroid hormone, TG is triglycerides.)

|     | $\text{K}^+$ | $\text{PO}_4^-$ | $\text{Ca}^{2+}$ | Hb | PTH | TG |
|-----|--------------|-----------------|------------------|----|-----|----|
| (A) | ↑            | ↓               | ↑                | ↓  | ↑   | ↓  |
| (B) | ↑            | ↑               | ↓                | ↓  | ↑   | ↑  |
| (C) | ↑            | ↑               | ↑                | ↓  | ↓   | ↑  |
| (D) | ↓            | ↓               | ↓                | ↑  | ↓   | ↓  |

**The answer is B: Increased  $\text{K}^+$ , Increased  $\text{PO}_4^-$ , Decreased  $\text{Ca}^{2+}$ , Decreased Hb, Increased PTH, Increased TG.** It is important to recognize and understand the changes that take place in chronic renal failure. Consider some of the important regulatory mechanisms of the kidneys (e.g., salt and water balance, RAAS, waste product secretion, role in vitamin D activation, role in erythropoiesis, etc.), and consider what the changes would be if they failed to work properly. Failure of the RAAS and other mechanisms of salt and water balance lead to fluid overload, hyponatremia, hyperkalemia, and hyperphosphatemia. Hypocalcemia is due to several factors: a loss in the active form of vitamin D (leading to decreased GI absorption and renal reabsorption), high serum phosphate levels, and metabolic acidosis (failure to excrete

daily acid load). As a response, serum PTH will be elevated (secondary hyperparathyroidism, which may lead to tertiary hyperparathyroidism with time); consistently elevated PTH will increase bone turnover and produce osteodystrophy. Other changes include anemia due to loss of erythropoietin (EPO) secretion by the kidneys, dyslipidemia (commonly hypertriglyceridemia), and hypertension. Uremia refers to the clinical syndrome that accompanies the elevation in BUN and creatinine and includes nausea, vomiting, anorexia, encephalopathy, pericarditis, and bleeding from platelet dysfunction.

11

A 66-year-old woman presents to her physician for her annual examination. Her medical history is significant for hypertension and osteopenia. She is compliant with her medications and takes benazepril and a daily multivitamin with high calcium and vitamin D. She does not smoke and does weight-bearing exercises 4 times weekly. She denies any falls or previous fractures. On examination, her blood pressure is 164/94 mmHg and her heart rate is 89 beats per minute.

Which of the following medications should be added to her current regimen?

- (A) Hydrochlorothiazide
- (B) Furosemide
- (C) Metoprolol
- (D) Alendronate

**The answer is A: Hydrochlorothiazide.** This patient has poorly controlled hypertension on an ACE inhibitor, and therefore the dose should be increased or another agent should be added. Because this woman also has osteopenia, a thiazide diuretic would be an excellent option due to its effect of increasing the reabsorption of calcium in the nephron. (B) Furosemide is a loop diuretic and would cause increased calcium excretion in the urine, and thus would not be a good option for this patient. (C) A  $\beta$ -blocker does not address any of the patient's comorbidities, and so a thiazide diuretic is a better option. (D) A bisphosphonate should be started if the patient has diagnosed osteoporosis (DEXA scan T-score  $\leq -2.5$ ) or a previous fragility fracture; this patient has osteopenia (DEXA scan T-score between  $-1$  and  $-2.5$ ).

12

A 57-year-old man presents to his physician for his annual examination. He has a history of hypertension, chronic obstructive pulmonary disease (COPD), and benign prostatic hyperplasia (BPH). On examination, there is hyper-resonance to percussion of both lung fields and a diffusely enlarged, nontender prostate on rectal examination. His blood work is unremarkable, but urine studies show 12 RBCs per high power field. There are no dysmorphic RBCs or RBC casts, and there are no other cells or protein. He denies any fevers, flank or groin pain, episodes of gross

hematuria, or dysuria. A repeat urinalysis 1 week later confirms the presence of microscopic hematuria, and his urine culture is negative. He elects to undergo further workup with a CT scan of the abdomen and pelvis with and without contrast, which is unremarkable.

What is the next step in management?

- (A) Measure PSA
- (B) Transrectal ultrasound and biopsy of the prostate
- (C) Intravenous pyelogram
- (D) Renal biopsy
- (E) Cystoscopy
- (F) Reassurance

**The answer is E: Cystoscopy.** Microscopic hematuria is defined as  $\geq 3$  RBCs per high power field on urine sediment microscopy, and should be confirmed with a repeat study given the high incidence of transient hematuria (which is usually benign but in older patients is still associated with an increased risk of malignancy). (D) Glomerulonephritis is a potential cause of hematuria and may lead to a renal biopsy if suspected, but in this case it is unlikely given that there were no dysmorphic RBCs, RBC casts, or other suggestive findings. In the absence of infection or glomerular disease, urine cytology (to screen for infections and neoplasms) and a CT scan (to screen for nephrolithiasis, renal neoplasms, etc.) should be performed. (C) An IV pyelogram may be used to visualize the urinary tract, but a CT scan is a better imaging modality and was already performed in this case. The next step is therefore cystoscopy, which will help to visualize the bladder for cancer. Remember that in microscopic hematuria, in the absence of an identifiable cause (infection or glomerular disease), all patients should receive radiologic imaging of the urinary tract and cystoscopy.

(A, B) This patient has a history of BPH and consistent findings on examination (diffusely enlarged prostate), making prostate cancer a less likely explanation for this patient's hematuria. PSA screening may be discussed with the patient in the future, but a cystoscopy needs to be performed next. (F) In the presence of BPH, new fragile blood vessels form and may rupture causing hematuria; however, more serious causes of hematuria still need to be ruled out.

13

The Internal Medicine service at a hospital requests that one of their patients receive dialysis. Which of the following is NOT an indication for dialysis?

- (A) End-stage renal disease ( $\text{GFR} < 15 \text{ mL/min}$ )
- (B) Hyperkalemia
- (C) Uremic pericarditis
- (D) Volume overload
- (E) Bleeding from uremia

**The answer is A: End-stage renal disease (GFR <15 mL/min).** The indications for dialysis can be remembered with the mnemonic *AEIOU*: Acidemia, Electrolyte disturbance (hyperkalemia, hyper- or hypocalcemia, hyperphosphatemia, hyperuricemia), Intoxication (e.g., salicylates, methanol), Overload of volume, and Uremic complications. End-stage renal disease, defined as a GFR <15 mL/min, is not itself an indication for dialysis. Uremia is the clinical syndrome that accompanies renal failure, and is characterized by a decrease in the excretion of water and electrolytes, a decrease in the secretion of organic solutes (e.g., nitrogenous waste products), and a decrease in renal hormone synthesis (e.g., EPO). Three complications of uremia are indications for dialysis: pericarditis/pleuritis, encephalopathy, and bleeding diathesis (due to platelet dysfunction). There are a few other indications that are not represented in the mnemonic, and these are hypertension refractory to medications, malnutrition, and persistent nausea and vomiting.



A 19-year-old girl is brought into an eating disorder clinic for a several year history of anorexia nervosa. She agrees to undergo an intensive inpatient rehabilitation service. She is started on a monitored feeding program, but after eating several meals she begins to feel nauseous and develops some edema. Her laboratory values are significant for a serum potassium level of 2.8 mEq/L, phosphorus level of 1.2 mg/dL, and magnesium level of 0.8 mEq/L.

Which of the following is the most serious complication that can result from this syndrome?

- (A) Heart failure
- (B) Respiratory failure
- (C) Renal failure
- (D) Central pontine myelinolysis

**The answer is A: Heart failure.** This patient has hypophosphatemia, hypokalemia, and hypomagnesemia, which are manifestations of the refeeding syndrome. This syndrome occurs after severely malnourished patients suddenly increase their nutritional intake, and treatment involves decreasing the level of nutritional intake and repleting important electrolytes and vitamins. The most concerning electrolyte change is the rapid decrease in serum phosphate. Whole body phosphate levels are depleted during the malnourished phase, and refeeding causes two things: increased utilization of phosphate to synthesize molecules such as ATP, and increased cellular uptake of phosphate as well as other electrolytes (e.g., potassium and magnesium). Hypophosphatemia can cause cardiac dysfunction leading to heart failure and possibly death. (B) Respiratory failure is another potential consequence of the refeeding syndrome, but can be addressed with mechanical ventilation. (C, D) Renal failure is not a common consequence

of the refeeding syndrome, and central pontine myelinolysis (now known as osmotic demyelination syndrome) is a consequence of an overly rapid correction of hyponatremia.

15

As part of a study, a healthy volunteer with no medical problems is asked to hyperventilate for a few minutes, after which laboratory values are drawn.

Which of the following findings would you expect?

|     | pH   | Anion gap | HCO <sub>3</sub> | PaCO <sub>2</sub> |
|-----|------|-----------|------------------|-------------------|
| (A) | 7.40 | Normal    | 24 mEq/L         | 40 mmHg           |
| (B) | 7.55 | Normal    | 22 mEq/L         | 25 mmHg           |
| (C) | 7.50 | Normal    | 14 mEq/L         | 24 mmHg           |
| (D) | 7.32 | Increased | 16 mEq/L         | 30 mmHg           |

**The answer is B: pH 7.55, Anion gap normal, HCO<sub>3</sub> 22 mEq/L, PaCO<sub>2</sub> 25 mmHg.** (A) Acute hyperventilation will produce a respiratory alkalosis, decreasing serum PaCO<sub>2</sub> and increasing the pH. (C) The serum bicarbonate will not decrease very much with acute respiratory alkalosis; the formal calculation for predicting the decrease in HCO<sub>3</sub> is:  $0.2 \times \Delta\text{PaCO}_2$  (predicts a drop in HCO<sub>3</sub> of 3.2 mEq/L; 14 mEq/L is therefore too low). (D) The presence of an anion gap indicates a metabolic acidosis, which would not be present as a result of hyperventilation.

16

A 28-year-old IV drug user presents to the hospital with shortness of breath. The murmur of tricuspid regurgitation is heard on cardiac auscultation, and a chest x-ray shows multiple opacities in both lungs. An echocardiogram confirms endocarditis, and the patient is started on empiric vancomycin and gentamicin while blood cultures are pending. Two days later, the following results are seen on her laboratory tests.

|                     |                                |
|---------------------|--------------------------------|
| Blood urea nitrogen | 28 mg/dL                       |
| Creatinine          | 1.8 mg/dL (baseline 0.9 mg/dL) |
| Urinalysis          | Pigmented granular casts       |

Which of the following should be done next?

- (A) IV fluids
- (B) Temporary hemodialysis
- (C) Stop gentamicin
- (D) Stop vancomycin
- (E) Immediate surgery of the infected valve

**The answer is C: Stop gentamicin.** This patient developed ATN, most likely as a consequence of using an aminoglycoside antibiotic. Pigmented

**Table 3-2    Differential Diagnosis of Renal Disease Based on Urinalysis**

| Finding                                        | Diagnosis                                                                                                                                                                                                                                                                                                                                                      |
|------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RBCs                                           | <ul style="list-style-type: none"><li>• Extrarenal causes most common: urinary tract cancers, infection, nephrolithiasis, trauma from catheter</li><li>• Intrarenal causes: glomerular disease, vascular disease, trauma, cancer, nephrolithiasis</li><li>• Positive blood on urine dipstick but no RBCs on urinalysis: hemoglobinuria/myoglobinuria</li></ul> |
| WBCs                                           | UTI, glomerulonephritis, AIN                                                                                                                                                                                                                                                                                                                                   |
| Protein                                        | Glomerular disease, tubular or interstitial damage, multiple myeloma, orthostatic proteinuria, transient (fever, exercise, etc.)                                                                                                                                                                                                                               |
| Dysmorphic RBCs or RBC casts                   | Glomerulonephritis                                                                                                                                                                                                                                                                                                                                             |
| WBC casts                                      | Glomerulonephritis, pyelonephritis, AIN                                                                                                                                                                                                                                                                                                                        |
| Pigmented granular casts ("muddy brown casts") | ATN                                                                                                                                                                                                                                                                                                                                                            |
| Hyaline and waxy casts                         | Nonspecific; <i>broad</i> waxy casts may indicate chronic renal failure                                                                                                                                                                                                                                                                                        |
| Fatty casts ("Maltese cross" appearance)       | Lipiduria from glomerular disease                                                                                                                                                                                                                                                                                                                              |
| AKI + calcium oxalate crystals                 | Ethylene glycol toxicity                                                                                                                                                                                                                                                                                                                                       |
| AKI + uric acid crystals                       | Tumor lysis syndrome                                                                                                                                                                                                                                                                                                                                           |



granular casts (“muddy brown casts”) on urinalysis are highly suggestive of ATN (Table 3-2), which can be caused by ischemia (progression of prerenal AKI) or toxins (medications, contrast, hemoglobin/myoglobin, crystals, and proteins such as light chains in multiple myeloma). Besides aminoglycosides, other important medications that can cause ATN include cisplatin, amphotericin, foscarnet, tenofovir, and contrast agents. Certain medications can also cause ATN by causing crystal formation; these include acyclovir, indinavir, and methotrexate. Treatment of ATN is largely supportive, and the first step of management is to remove the offending agent (in this case, gentamicin). (D) Vancomycin can be continued, which will cover MSSA and MRSA since *S. aureus* is the most common cause of endocarditis in IV drug users. Antibiotic therapy can be tailored to the blood culture results once they are available. (Note: There is some controversy about vancomycin causing AKI, but certainly gentamicin would be the first medication to stop.)

(A) IV fluids would be the correct answer if this patient’s ATN were a result of advanced prerenal disease from hypovolemia; however, it is more likely to be toxin-induced ATN. (B) This patient does not meet any indications for dialysis (Question 13) from the information provided. (E) Septic emboli can travel from left-sided vegetations (mitral or aortic valves) and cause renal failure; however, this patient has right-sided disease (hence the septic emboli to the lungs).

**17** A 76-year-old man is hospitalized for pneumonia and was started on empiric antibiotics. He developed a rash in response to the antibiotics, and the symptoms were somewhat relieved with diphenhydramine. Several days after this, the patient developed oliguria. His laboratory values are shown below.

|                     |                                |
|---------------------|--------------------------------|
| Sodium              | 138 mEq/L                      |
| Potassium           | 4.8 mEq/L                      |
| Chloride            | 108 mEq/L                      |
| Bicarbonate         | 20 mEq/L                       |
| Blood urea nitrogen | 18 mg/dL                       |
| Creatinine          | 1.6 mg/dL (baseline 1.1 mg/dL) |
| Glucose             | 114 mg/dL                      |

A urinalysis is unremarkable. A renal ultrasound shows bilateral dilation of the renal pelvis and calyces.

Which of the following is the most likely anatomic site of obstruction in this patient?

- (A) Renal arteries
- (B) Ureters
- (C) Renal tubules
- (D) Bladder
- (E) Renal veins
- (F) Ureteropelvic junction

**The answer is D: Bladder.** The abrupt onset of oliguria with a rise in creatinine indicates AKI, and the renal ultrasound showing hydronephrosis limits the differential diagnosis to postrenal AKI (obstructive nephropathy). An important historical clue given in the vignette is the administration of diphenhydramine, which is an antihistamine that also has anticholinergic properties. Elderly patients are often very sensitive to anticholinergics, and can experience adverse reactions such as confusion and urinary retention. Urinary retention results from the failure of the detrusor muscle to cause bladder contraction, since it contracts via cholinergic stimulation. Patients with BPH, which is a common diagnosis in older men, may also experience postrenal AKI with anticholinergics. This patient should have a urethral or suprapubic catheter placed to decompress the bladder and urinary tract.

(A, C, E) An obstruction in the renal arteries, tubules, or veins would cause renal injury but would not cause an obstruction in the urinary tract leading to hydronephrosis. (B, F) The ureters and ureteropelvic junction are common places for kidney stones to become lodged; however, it is important to know that AKI from ureteral obstruction occurs only if the obstruction is bilateral. This is due to the fact that obstruction of one ureter decreases the filtration rate of that kidney, but the other kidney will increase its GFR to compensate. It would be unlikely for two kidney stones to become lodged at the same time in this patient. Besides BPH and anticholinergic medications, other important causes of obstructive nephropathy include retroperitoneal fibrosis, neurogenic bladder (e.g., spinal cord injury), and malignancy (e.g., prostate cancer, abdominal cancer compressing the urinary tract, etc.).

**18** A 63-year-old man complains of persistent abdominal pain for several weeks. In addition, he endorses an unintentional weight loss of 10 kg over the past few months. His medical history is significant for hypertension and diabetes. He has a 45 pack-year smoking history and drinks alcohol moderately. His hemoglobin is found to be 18.8 g/dL, and his urinalysis shows 23 RBCs per high power field. A CT scan is performed and shows a large mass within the left kidney.

Besides erythrocytosis, what is another potential complication of this disease?

- (A) Limbic encephalitis
- (B) Muscle weakness and double vision
- (C) Hypercalcemia
- (D) Hyponatremia

**The answer is C: Hypercalcemia.** Renal cell carcinoma (RCC) is the most common malignancy affecting the kidneys. The “classic triad” of RCC is flank pain, abdominal mass, and hematuria; however, these three symptoms/signs are rarely seen together in the same patient. The diagnosis is suggested by the patient’s risk factors (age, hypertension, smoking), laboratory findings (erythrocytosis, hematuria), and CT scan showing a renal mass. Anemia is actually much more common in RCC than erythrocytosis, but erythrocytosis is a potential paraneoplastic syndrome (when EPO is secreted and functional; the majority of tumors will secrete nonfunctional EPO, which is why anemia is more common). Other important paraneoplastic syndromes associated with RCC include hypercalcemia from parathyroid hormone-related protein (PTHrP) secretion, thrombocytosis, secondary amyloidosis, polymyalgia rheumatica, and liver disease (Stauffer syndrome).

(A) Limbic encephalitis is an autoimmune process affecting the medial temporal lobes or limbic structures that presents with confusion, memory impairment, and/or seizures, and it may be paraneoplastic or nonparaneoplastic. In cases of paraneoplastic limbic encephalitis, it is most commonly associated with small cell lung cancer (SCLC), testicular and thymic tumors, breast cancer, and Hodgkin lymphoma. (B) Muscle weakness and double vision suggests a neuromuscular disorder such as myasthenia gravis, which is most commonly associated with thymic tumors. (D) Hyponatremia caused by the syndrome of inappropriate ADH (SIADH) is associated with SCLC, other extrapulmonary small cell cancers, and head and neck cancers.

19

A 28-year-old man presents to his physician with complaints of fatigue and muscle cramps that have developed slowly over the past few months. In addition, he says that he often needs to get up in the middle of the night to urinate. He has no significant past medical history or family history, does not take any medications or supplements, eats a regular diet, and does not smoke, drink alcohol, or use illicit drugs. He denies any recent illnesses, vomiting, or diarrhea. His temperature is 36.8°C, blood pressure is 102/68 mmHg, heart rate is 82 beats per minute, and respiratory rate is 10 breaths per minute. His laboratory values and urine studies are shown below.

|                     |                         |
|---------------------|-------------------------|
| Sodium              | 136 mEq/L               |
| Potassium           | 2.6 mEq/L               |
| Chloride            | 93 mEq/L                |
| Bicarbonate         | 34 mEq/L                |
| Blood urea nitrogen | 9 mg/dL                 |
| Creatinine          | 0.8 mg/dL               |
| Glucose             | 150 mg/dL (non-fasting) |
| Magnesium           | 0.6 mEq/L               |
| Arterial blood gas  |                         |
| pH                  | 7.50                    |
| PaO <sub>2</sub>    | 95 mmHg                 |
| PaCO <sub>2</sub>   | 48 mmHg                 |

Urine studies show high levels of potassium and chloride, and low levels of calcium.

Which of the following conditions would produce similar findings to this patient's disease?

- (A) Chronic diarrhea
- (B) Adrenal aldosterone-secreting tumor
- (C) Chronic chlorthalidone use
- (D) Chronic furosemide use

**The answer is C: Chronic chlorthalidone use.** This patient has Gitelman syndrome, a rare autosomal recessive disease caused by a defect in the thiazide-sensitive sodium–chloride cotransporter in the nephron. The effect is similar to the chronic use of a thiazide diuretic, and often presents in early adulthood with hypokalemia, metabolic alkalosis, hypomagnesemia, and a low blood pressure. (D) Bartter syndrome is a similar genetic disease but mimics the chronic use of a loop diuretic such as furosemide, bumetanide, or ethacrynic acid. Thus, urine calcium levels can help to differentiate between Bartter and Gitelman syndromes. Treatment of both Bartter and Gitelman syndromes is with a potassium-sparing diuretic (e.g., spironolactone, amiloride) that will help correct the hypokalemia, hypomagnesemia, and metabolic alkalosis. Though the reader may not have been familiar with the diagnosis, they are expected to know that thiazide diuretics can cause all of the same findings.

(A) Chronic diarrhea will produce hypokalemia with a metabolic *acidosis* due to GI loss of potassium and bicarbonate. Surreptitious vomiting and diuretic abuse, on the other hand, present similarly to Bartter and Gitelman syndromes. Surreptitious vomiting will have a low urine chloride ( $<20$  mEq/L). (B) Both Bartter and Gitelman syndromes produce a hyper-renin–hyperaldosterone state in response to chronic volume contraction; however, primary hyperaldosteronism from an adrenal tumor will present with hypertension and low renin.

20

A 53-year-old man with a history of diabetes and diabetic nephropathy is undergoing workup for a suspected diagnosis of coronary artery disease. His exercise stress test results place him in the high risk category, and he elects to undergo further workup with coronary angiography. The procedure was uneventful, and 2 days later he has laboratory tests drawn that are significant for a creatinine of 1.9 mg/dL (baseline 1.3 mg/dL). The serum leukocyte count, as well as the differential, is normal. A urinalysis shows pigmented granular casts with no RBCs or white blood cells (WBCs), and a FENa is calculated at 0.85%. The patient denies any flank pain or dysuria, and his vitals, physical examination, and urine output are normal.

Which of the following is the most likely diagnosis?

- (A) Reaction to a contrast agent
- (B) Renal atheroemboli
- (C) Prerenal acute kidney injury
- (D) Acute interstitial nephritis
- (E) Acute tubular necrosis from renal ischemia

**The answer is A: Reaction to a contrast agent.** Patients with a history of CKD (especially diabetic CKD) are at an increased risk of contrast-induced nephropathy. The onset is typically 24 to 48 hours after the contrast agent is administered, and patients will usually have a mildly increased creatinine without oliguria. Contrast agents are thought to produce ATN as a result of direct toxic effects as well as renal vasoconstriction. Most cases are reversible. Pretreating at-risk patients can reduce the risk of this complication; options include IV fluids ( $\pm$  bicarbonate) and N-acetylcysteine.

(B) Atheroembolic events are a potential complication of angiography, and should be considered in the differential diagnosis. However, the absence of eosinophilia and other embolic phenomena (e.g., ischemia of several toes) makes this diagnosis less likely. (C) Although a FENa  $<1\%$  is typical of prerenal AKI and a FENa  $>2\%$  is typical of ATN, contrast-induced nephropathy typically produces a FENa  $<1\%$ . (D) The absence of other cells or casts (especially WBCs) on urinalysis makes acute interstitial nephritis (AIN) very unlikely. In addition, AIN would most likely produce a FENa  $>2\%$ . (E) The pigmented granular casts on urinalysis confirm ATN, but ischemia- or

toxin-induced ATN would have a FENa >2%, so this is not the best answer choice.

**21** A middle-aged woman is diagnosed with hypertension and counseled about starting an antihypertensive medication. The patient agrees to start hydrochlorothiazide, but wants to know about potential side effects that she might experience.

Which of the following is a potential adverse effect of this medication?

- (A) Hyperkalemia
- (B) Hypercholesterolemia
- (C) Hypoglycemia
- (D) Hypocalcemia

**The answer is B: Hypercholesterolemia.** Thiazide diuretics (e.g., hydrochlorothiazide, chlorthalidone) are common agents used for hypertension and work by blocking the sodium–chloride cotransporter in the distal convoluted tubule. The adverse effects of these agents, as well as other classes of diuretics are extremely high yield for the shelf examination. It is important to know that excessive diuresis can produce hypotension as well as electrolyte and metabolic abnormalities. Hypercholesterolemia is one of the important adverse effects of thiazide diuretics. (A, C, D) Thiazide diuretics may also cause hypokalemia, hyperglycemia, and hypercalcemia, so these answer choices are opposites. Other important effects include hyponatremia, hypomagnesemia, hyperuricemia (consider this in patients with gout), metabolic alkalosis, and a cross-sensitivity in patients with a sulfa allergy (causing a skin rash, AIN, etc.).

Loop diuretics (e.g., furosemide, bumetanide, ethacrynic acid) work by blocking the sodium–potassium–chloride ( $\text{Na}^+/\text{K}^+/2\text{Cl}^-$ ) cotransporter in the loop of Henle. Important adverse effects include the same electrolyte changes as in thiazides (except *hypocalcemia* instead of hypercalcemia), hyperuricemia, metabolic alkalosis, hypersensitivity reactions, and ototoxicity. Potassium-sparing diuretics work on principal cells of the nephron to block either aldosterone receptors (e.g., spironolactone, eplerenone) or aldosterone-sensitive sodium channels (e.g., amiloride, triamterene). High yield adverse effects of these agents include hyperkalemia and metabolic acidosis. Spironolactone can cause agranulocytosis and also acts as an antiandrogen and can produce effects such as gynecomastia. Eplerenone is more selective for the mineralocorticoid receptor and therefore does not cause gynecomastia.

**22** A 28-year-old woman presents to her physician complaining of abdominal pain. A urinalysis shows 8 RBCs with no WBCs or protein, and no dysmorphic cells or casts. She is eventually diagnosed with gastroenteritis and is sent home. A urine culture comes back negative several days later.

What should be done next in the workup of this patient with hematuria?

- (A) Transvaginal ultrasound
- (B) CT scan of the abdomen and pelvis
- (C) Cystoscopy
- (D) Repeat urinalysis in a few days
- (E) Reassurance

**The answer is D: Repeat urinalysis in a few days.** This patient has microscopic hematuria that has no obvious relationship to the given diagnosis of gastroenteritis. There are many causes of hematuria, but hematuria is usually transient and benign in younger patients. Fever and exercise are examples of common causes of benign transient hematuria; however, the cause is often not determined. In addition, the menstrual history of this woman is not given, and this could also be the cause. Before any invasive procedures are performed, it would be wise to repeat a urinalysis to see if this patient has either transient or persistent hematuria. (B, C) Cystoscopy and a CT scan may be helpful in the workup of persistent hematuria; however, it should be confirmed as persistent first. (E) Given that malignancy is a potential cause of persistent microscopic hematuria, reassurance should only be offered after the urinalysis is repeated.

23

A 62-year-old woman presents to the Emergency Department because of new onset swelling and tea-colored urine. She has a history of GERD, but reports being healthy otherwise. She had a fever and sore throat 2 weeks ago but did not see a physician at that time. Currently she is afebrile with a blood pressure of 158/96 mmHg and a heart rate of 89 beats per minute. She has generalized edema with a normal cardiac examination. Her creatinine is 1.6 mg/dL (baseline 0.9 mg/dL), and urine dipstick shows 3+ blood and 2+ protein with WBCs and dysmorphic RBCs.

What would you expect the rest of her laboratory results to be? (Note: ANA is antinuclear antibody, ANCA is antinuclear cytoplasmic antibody, and ASO is antistreptolysin O antibody.)

|     | ANA      | ANCA     | ASO      | C3     | C4     |
|-----|----------|----------|----------|--------|--------|
| (A) | Negative | Negative | Negative | Normal | Normal |
| (B) | Negative | Negative | Positive | Low    | Normal |
| (C) | Positive | Negative | Negative | Low    | Low    |
| (D) | Negative | Positive | Negative | Normal | Normal |

**The answer is B: Negative ANA, Negative ANCA, Positive ASO, Low C3, Normal C4.** A patient presenting with nephritic syndrome (gross hematuria with proteinuria and dysmorphic RBCs), acute kidney injury, and a recent sore throat suggests poststreptococcal glomerulonephritis. Although the diagnosis might not have been particularly challenging, the reader must know the expected laboratory findings in this condition. In most patients, ASO antibodies will be positive indicating a recent strep infection, and C3 will be low with a normal or mildly low C4. The mechanism of this disease most likely involves *in situ* immune complex formation within the glomeruli in response to deposited streptococcal antigens, which will activate the alternative complement pathway. (C) In contrast, SLE will cause the activation of the classical complement pathway, causing low C3 and C4. (D) The history of a recent sore throat makes poststreptococcal glomerulonephritis more likely than ANCA-positive glomerulonephritides such as granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome).

For patients with possible glomerulonephritis, it is first useful to rule out conditions that may mimic glomerulonephritis (Figure 3-4). Criteria or evidence for nephrotic or nephritic syndrome should then be assessed, and if

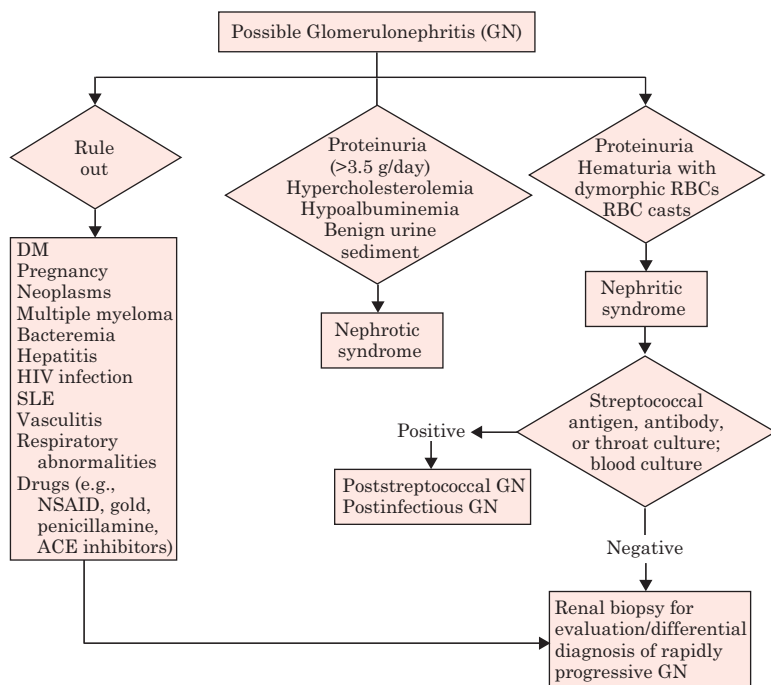


Figure 3-4



the cause is not readily apparent then a renal biopsy may be indicated for the diagnosis.

24

A 38-year-old woman with SLE presents with shortness of breath. The symptoms began acutely 2 hours ago and occurred while at rest. On examination, she has a blood pressure of 102/70 mmHg, heart rate of 112 beats per minute, and respiratory rate of 24 breaths per minute. She appears weak and is diffusely edematous. A CT angiogram confirms pulmonary embolism, and further workup reveals renal vein thrombosis. Her laboratory values and workup are shown below.

|                     |                        |
|---------------------|------------------------|
| Sodium              | 142 mEq/L              |
| Potassium           | 3.9 mEq/L              |
| Chloride            | 114 mEq/L              |
| Bicarbonate         | 18 mEq/L               |
| Blood urea nitrogen | 14 mg/dL               |
| Creatinine          | 1.0 mg/dL              |
| Albumin             | 1.8 g/dL               |
| Urinalysis          | 4+ protein, waxy casts |

Which of the following is the most likely condition that increased this patient's risk for pulmonary embolism?

- (A) Minimal change disease
- (B) Focal segmental glomerulosclerosis
- (C) Membranoproliferative glomerulonephritis
- (D) IgA nephropathy
- (E) Membranous nephropathy
- (F) Chronic pyelonephritis
- (G) Alport syndrome
- (H) Granulomatosis with polyangiitis

**The answer is E: Membranous nephropathy.** This patient has nephrotic syndrome, as evidenced by her proteinuria, hypoalbuminemia, edema, and lipiduria (waxy casts). Patients with nephrotic syndrome are in a hypercoagulable state and can form clots in the arterial and venous circulations. This is partly due to urinary losses of antithrombin and plasminogen. Renal vein thrombosis is a potential complication of nephrotic syndrome and can be

chronic, potentially manifesting with pulmonary embolism. The most common type of nephrotic syndrome associated with thrombotic complications is membranous nephropathy, typically with very high levels of proteinuria ( $>10$  g/d). About 10% to 20% of lupus patients develop membranous nephropathy, and having lupus in addition to membranous nephropathy further increases the risk of renal vein thrombosis. (A, B, C) These conditions are causes of nephrotic syndrome but are less associated with thrombotic complications than membranous nephropathy. Membranoproliferative glomerulonephritis can also cause nephritic syndrome. (D, G, H) These are causes of nephritic syndrome (although Alport syndrome can also present with nephrotic syndrome). (F) Chronic pyelonephritis (e.g., xanthogranulomatous pyelonephritis) will not present with nephrotic range proteinuria but will present with urine studies suggestive of an infection (e.g., WBCs, leukocyte esterase, etc.).



The police brought a 32-year-old man to the Emergency Department. He is extremely disheveled and appears inebriated, making it difficult to obtain a history. On examination, there is horizontal gaze nystagmus but no afferent pupillary defect. He also has tenderness along the right flank. His laboratory values are shown below.

|                     |                                     |
|---------------------|-------------------------------------|
| Sodium              | 137 mEq/L                           |
| Potassium           | 5.2 mEq/L                           |
| Chloride            | 105 mEq/L                           |
| Bicarbonate         | 10 mEq/L                            |
| Blood urea nitrogen | 24 mg/dL                            |
| Creatinine          | 1.5 mg/dL                           |
| Glucose             | 138 mg/dL                           |
| Urinalysis          | Many RBCs, calcium oxalate crystals |

The patient is found to have a high serum osmolal gap. The patient's airway is secured, and he is placed on mechanical ventilation.

What should be done next in the management of this patient?

- (A) Activated charcoal
- (B) N-acetylcysteine
- (C) Glucagon
- (D) Fomepizole
- (E) Flumazenil

**The answer is D: Fomepizole.** The patient in this vignette appears to have alcohol intoxication with flank pain, hematuria, and calcium oxalate crystals on urinalysis. In addition, he has an anion gap metabolic acidosis and a high serum osmolal gap, which are all important signs of ethylene glycol intoxication. Methanol intoxication may mimic this presentation, but the metabolic byproducts of methanol cause optic nerve damage (causing an afferent pupillary defect) whereas the metabolic byproducts of ethylene glycol are more likely to cause renal failure. The presence of calcium oxalate crystals may be seen in ethylene glycol intoxication, but it is a nonspecific finding and should not be relied upon to make the diagnosis. Fomepizole is a competitive aldehyde dehydrogenase inhibitor that prevents the breakdown of methanol and ethylene glycol into their toxic byproducts. (Note: ethanol is another effective competitive inhibitor that was used historically, but fomepizole is preferred.) Other important treatments are bicarbonate and hemodialysis, especially if the patient has significant acidemia. **(A, B)** Activated charcoal is not beneficial with any type of alcohol intoxication; however, it should be used in acetaminophen toxicity followed by N-acetylcysteine (if the patient meets criteria based on serum levels plotted on the nomogram). **(C, E)** Glucagon is used for  $\beta$ -blocker toxicity, and flumazenil is used for benzodiazepine toxicity.

26

A 49-year-old man presents to his physician for a routine examination and is found to be hypertensive. He has no past medical history, and his family history is unknown since he was adopted. Blood work shows a BUN and creatinine of 21 mg/dL and 1.6 mg/dL, respectively. Abdominal ultrasound shows bilaterally enlarged kidneys with many cysts.

Which of the following is NOT a potential complication of this disease?

- (A)** Hypertension
- (B)** Renal cell carcinoma
- (C)** Subarachnoid hemorrhage
- (D)** Development of hepatic cysts
- (E)** Aortic regurgitation

**The answer is B: Renal cell carcinoma.** Autosomal dominant polycystic kidney disease (ADPKD) is caused by a mutation in the PKD1 (more common) or PKD2 genes and causes progressive renal disease starting most commonly in the fourth decade. There is usually a positive family history, so many patients are diagnosed early with a screening ultrasound (or other imaging modality) that shows multiple large cysts in both kidneys. **(D)** Hepatic and pancreatic cysts can also develop. **(A)** Any cause of renal failure will produce hypertension. Treatment with ACE inhibitors or ARBs, along with control of hypertension, can slow down the progression of the disease but there is no cure for the disease. **(C)** The most concerning extrarenal complication of ADPKD is cerebral aneurysms, which can rupture and cause intracerebral or subarachnoid

hemorrhage. (E) Valvular disease is also very common in these patients, especially mitral valve prolapse and aortic regurgitation. (B) Pancreatic cysts may slightly increase the risk of certain types of pancreatic cancer, but ADPKD is not associated with an increased risk of renal cell carcinoma.

27

A 58-year-old woman is referred to an ophthalmologist because of vision loss. She describes previous episodes of acute vision impairment that gradually improved over days. An image of her retina is shown in Figure 3-5.



**Figure 3-5**

If this patient were to undergo renal biopsy, what are the pathologic findings associated with this disease?

- (A) Nodular glomerulosclerosis, mesangial expansion, and basement membrane thickening
- (B) Scattered crescentic lesions with fibrin and plasma proteins
- (C) Vascular intimal thickening and hyaline deposition
- (D) Subepithelial immune complex deposits

**The answer is A: Nodular glomerulosclerosis, mesangial expansion, and basement membrane thickening.** Although it is unlikely that the Medicine shelf examination will require interpretation of fundoscopic images, this question makes a few important points about diabetes. First, diabetic retinopathy is extremely common and is a major cause of blindness. There are proliferative (neovascularization of the retina) and nonproliferative forms, with common features of microaneurysms, flame hemorrhages, dot-blot hemorrhages, soft exudates (“cotton wool spots”), and macular edema. There is a large amount of hard exudates seen in the image above, which is caused by the leakage and deposition of lipid and protein from the retinal vessels. Some diabetic patients with

advanced ophthalmologic findings will have diabetic nephropathy; however, retinopathy often precedes nephropathy, so that diagnosis of diabetic retinopathy with a simple fundoscopic examination can herald the onset of other microvascular complications. The correct answer to the question is identifying the three pathologic features of diabetic nephropathy, which is answer choice **A**. Nodular glomerulosclerosis lesions are also referred to as Kimmelstiel–Wilson lesions.

**(B)** These findings are seen in RPGN, with causes including granulomatosis with polyangiitis, microscopic polyangiitis, and Goodpasture syndrome. **(C)** These are the pathologic findings of hypertensive nephrosclerosis, another very common cause of CKD. **(D)** Subepithelial immune complex deposits are seen in poststreptococcal glomerulonephritis.

28

A 62-year-old woman presents to the Emergency Department after experiencing gross hematuria and passing several blood clots in the urine. She denies any abdominal pain. Eventually a cystoscopy is performed, which confirms the suspected diagnosis of urothelial cancer of the bladder.

Which of the following is the most important risk factor for this condition?

- (A)** Smoking
- (B)** Exposure to benzene
- (C)** Exposure to aniline dyes
- (D)** Chronic cystitis

**The answer is A: Smoking.** Transitional cell (urothelial) bladder cancer is the most common urinary tract cancer, and smoking accounts for approximately half of the cases. If ever in doubt, smoking is always a good answer on the shelf examination. **(B, C)** There are many occupational exposures that increase the risk of bladder cancer, such as benzene, aniline dyes, diesel fumes, and so forth. **(D)** Anything that causes chronic inflammation of the urothelium will increase the risk of bladder cancer, but not to the degree that smoking does. Other important risk factors for malignancies of the urinary tract include a history of gross hematuria, analgesic abuse, radiation, and cyclophosphamide.

29

A 59-year-old woman presents to the Emergency Department complaining of severely painful skin lesions in the abdomen and thighs. Her medical history is significant for hypertension, hyperlipidemia, and end-stage renal disease. She has an arteriovenous fistula and undergoes hemodialysis 3 times weekly. She denies any recent medication changes or any illicit drug abuse, and denies ever taking warfarin. She is afebrile with a blood pressure of 162/96 mmHg and a heart rate of 96 beats per minute. On physical examination, there are areas of livedo reticularis over the abdomen with subcutaneous nodules and several necrotic ulcerations with eschar on both thighs (*Figure 3-6*). Her distal pulses are 2+ in all four extremities.



**Figure 3-6**

A review of her laboratory records over the past few months shows an uptrending calcium-phosphate product.

Which of the following is the most likely diagnosis?

- (A) Henoch-Schönlein purpura
- (B) Calcific uremic arteriolopathy
- (C) Necrotizing fasciitis
- (D) Deep venous thrombosis
- (E) Nephrogenic systemic fibrosis

**The answer is B: Calcific uremic arteriolopathy.** Also known as calciphylaxis, calcific uremic arteriolopathy is a devastating complication of end-stage renal disease (although it can rarely occur in patients without renal disease). Though there is vascular calcification that occurs in every patient with end-stage renal disease, calcific uremic arteriolopathy is a separate process that portends a poor prognosis. There is debate over the exact pathophysiology, but it is associated with an increased or uptrending calcium-phosphate product (serum calcium  $\times$  serum phosphate), elevated PTH, and high vitamin D doses. A skin biopsy confirms the diagnosis and shows medial calcification and subintimal fibrosis without any evidence of a vasculitis. (Note: important electrolyte and metabolic disturbances in end-stage renal disease include hyperkalemia, hypocalcemia, hyperphosphatemia, metabolic acidosis, secondary hyperparathyroidism that can progress to tertiary hyperparathyroidism, and renal osteodystrophy.)

(A) Henoch-Schönlein purpura is a small-vessel vasculitis that presents with palpable purpura of the lower extremities and buttocks, abdominal

pain, hematuria, and arthralgias. The patient's lesions are necrotic, and the vignette does not suggest hematuria or arthralgias. (C) Necrotizing fasciitis would present with fever, a rapidly expanding and erythematous lesion, and possibly local crepitation of the skin. (D) The onset of deep venous thrombosis is typically not symmetric, and would not cause necrotizing skin lesions. (E) Nephrogenic systemic fibrosis typically occurs after exposure to gadolinium contrast in patients with renal failure. The fibrotic skin lesions progress distally to proximally, leading to a "woody" appearance of the skin. Early calcific uremic arteriolopathy may resemble nephrogenic systemic fibrosis, but not after the necrotic ulcers develop.

30

A 29-year-old man with no significant medical history complains of tea-colored urine. He reports that he "just got over a cold." He denies any current fever, weight loss, flank pain, abdominal pain, or new sexual contacts. These symptoms have occurred twice before and have self-resolved without any treatment. He is afebrile with normal vitals, and his examination is unremarkable. Laboratory tests are drawn, which show a BUN of 14 mg/dL and a creatinine of 1.1 mg/dL. A urinalysis shows 2+ blood.

Which of the following is the most appropriate next step in management?

- (A) Observation
- (B) ACE inhibitor or ARB
- (C) Corticosteroids
- (D) Renal biopsy

**The answer is A: Observation.** IgA nephropathy (Berger disease) is the most common cause of primary glomerulonephritis in the developed world. The most common clinical presentation is recurrent gross hematuria that follows an upper respiratory tract infection, although many patients have microscopic hematuria  $\pm$  proteinuria that is discovered on routine urinalysis. On histology, there is deposition of IgA in the mesangium and glomerular capillary wall on immunofluorescence. The course of the disease is typically slow; half of patients will progress to end-stage renal disease over >20 years' time. However, IgA nephropathy may be associated with other glomerular diseases and some patients may develop RPGN. (D) Renal biopsy is used to confirm the diagnosis, but not all patients require biopsy. A biopsy may be useful if the patient has significant proteinuria, AKI (elevated creatinine), or hypertension. Patients without these findings like the one in this vignette can be observed without treatment and do not require renal biopsy. Repeat urine studies should be performed in 6 to 12 months. (B) If the patient developed significant proteinuria, then an ACE inhibitor or ARB would be useful to decrease the proteinuria and slow down the progression of the disease. (C) Corticosteroids may be used in patients with more severe disease.

**31** A 36-year-old African American man presents to the Emergency Department with new onset body swelling. He has a history of HIV and is taking antiretrovirals and trimethoprim-sulfamethoxazole for prophylaxis. His last CD4 count was 125 cells/mm<sup>3</sup>. His temperature is 38.2°C, blood pressure is 168/98 mmHg, heart rate is 94 beats per minute, and respiratory rate is 24 breaths per minute. Laboratory workup reveals a creatinine of 1.8 mg/dL, and a urine dipstick shows 4+ protein.

What is most likely to be seen on renal biopsy under light microscopy?

- (A) Normal appearing glomeruli
- (B) Diffuse thickening of the glomerular basement membrane
- (C) Splitting of the glomerular basement membrane
- (D) Collapsed and sclerotic glomeruli surrounded by normal glomeruli

**The answer is D: Collapsed and sclerotic glomeruli surrounded by normal glomeruli.** FSGS is one of the most common causes of nephrotic syndrome, and it is the most common cause in both black patients and in HIV patients. The diagnosis can be made with a renal biopsy that shows focal (only affecting some glomeruli) and segmental (only affecting part of a glomerulus) sclerosis. In HIV, the most common histologic variant is the collapsing form of FSGS. It is important to recognize that FSGS is a common cause of the nephrotic syndrome, especially in black patients and HIV patients.

(A) Minimal change disease will show normal appearing glomeruli under light microscopy and epithelial foot process fusion under electron microscopy. (B) This pathologic finding is seen with membranous nephropathy. (C) This finding is seen in Alport syndrome, which is caused by a mutation in type IV collagen.

**32** A 19-year-old college student develops fever, headache, and nuchal rigidity. Cerebrospinal fluid (CSF) cultures grow *Neisseria meningitidis*. She receives appropriate treatment, and her close contacts are given prophylactic antibiotic treatment. Her mother, who took this prophylactic treatment, developed a fever and maculopapular rash afterward. She is brought to the Emergency Department, and her laboratory values are shown below.

|            |                                |
|------------|--------------------------------|
| Sodium     | 133 mEq/L                      |
| Potassium  | 5.4 mEq/L                      |
| Creatinine | 2.1 mg/dL (baseline 1.0 mg/dL) |
| Urinalysis | WBC casts and eosinophils      |



Which of the following represents the likely antibiotic and complication that the mother experienced?

|     | Antibiotic Used               | Complication                       |
|-----|-------------------------------|------------------------------------|
| (A) | Ceftriaxone                   | Cholesterol emboli syndrome        |
| (B) | Rifampin                      | Acute interstitial nephritis       |
| (C) | Ciprofloxacin                 | Acute tubular necrosis             |
| (D) | Trimethoprim–sulfamethoxazole | Stevens–Johnson syndrome           |
| (E) | Rifampin                      | Antibiotic-resistant meningococcus |

**The answer is B: Rifampin, Acute interstitial nephritis.** There are several recommended prophylactic drugs for close contacts of a patient with bacterial meningitis from *N. meningitidis*: rifampin, ciprofloxacin, and ceftriaxone. (D) Trimethoprim–sulfamethoxazole is therefore not a correct option. The next step is identifying the complication that the mother experienced. She developed an abrupt rise in creatinine (AKI) with a rash; her urine studies showed WBCs and eosinophils. Taken together, the correct diagnosis is AIN, which is a type of intrinsic renal AKI. Though it is rare to see all of these symptoms together, drug-induced AIN may produce fever, rash, arthralgias, and/or eosinophilia/eosinophiluria. It is characterized by inflammatory cell infiltrates in the renal interstitium, and the most common cause is an allergic reaction to medications. There are many antibiotics that can cause this, and all of the ones listed above can cause it. Methicillin is not used as an antibiotic anymore, but it has a very high incidence of AIN. Other etiologic medications include NSAIDs, PPIs, cimetidine, diuretics, and allopurinol.

Besides medications, other causes of AIN include infections (e.g., *Legionella*, cytomegalovirus, tuberculosis; pyelonephritis can cause both an acute and chronic AIN) and systemic conditions (e.g., sarcoidosis, SLE, Sjögren syndrome, IgG4-related disease, lymphoma, leukemia, and others). Withdrawal of the offending agent is the first step in managing AIN; if the patient fails to respond, renal biopsy may aid in the diagnosis and assess the extent of damage, and corticosteroids may be beneficial. The only answer choice that includes AIN is B, and rifampin is an appropriate prophylactic treatment for close contacts. (Of note, rifampin is also the prophylactic treatment of choice for close contacts of invasive *H. influenzae* type B infection.)

(A) Urine eosinophils and rash may be seen in cholesterol emboli syndrome, but ceftriaxone does not cause this. (C) ATN would most likely show muddy brown casts on urinalysis. (E) Meningococcemia occurs with

or without concurrent meningitis and often presents with a petechial rash (not maculopapular) and systemic toxicity. WBC casts and eosinophiluria suggest the diagnosis of AIN, not meningococcemia.



A 49-year-old woman is hospitalized for pneumonia. She is managed appropriately and laboratory values are drawn. She has no past medical history, and a complete blood count and chemistry panel from 1 year ago were normal. Her laboratory values from this hospitalization are shown below.

|                     |           |
|---------------------|-----------|
| Sodium              | 136 mEq/L |
| Potassium           | 5.2 mEq/L |
| Chloride            | 105 mEq/L |
| Bicarbonate         | 20 mEq/L  |
| Blood urea nitrogen | 38 mg/dL  |
| Creatinine          | 1.9 mg/dL |
| FENa                | 2.5%      |

What is the most likely cause of this patient's renal disease?

- (A) Pyelonephritis
- (B) Renal ischemia
- (C) Acute interstitial nephritis
- (D) Embolic phenomenon
- (E) Goodpasture syndrome
- (F) Urinary tract obstruction
- (G) Acute tubular necrosis
- (H) Fibromuscular dysplasia

**The answer is G: Acute tubular necrosis.** This question tests the reader's knowledge of the most common cause of intrinsic renal AKI. Because the details in the vignette are quite limited, many of the answers could be the true diagnosis. However, on the shelf examination there are often similar questions that require the reader to "play the odds" and pick the most common cause. In this case, it is important to know that prerenal causes and ATN make up the majority of AKI cases in hospitalized patients. The FENa >2% indicates that this is intrinsic renal disease, and therefore the correct answer is ATN.

(A, C) Pyelonephritis is a cause of AIN; however, AIN is not the most common cause of intrinsic renal AKI. AIN might have been selected since

the patient likely took antibiotics for pneumonia; however, many antibiotics cause ATN as well. (B) Prerenal AKI from renal ischemia would be the correct answer if the FENa was  $<1\%$ . (D) Cholesterol emboli syndrome usually occurs after catheterization procedures involving the aorta and would be suggested by a rash and urine eosinophils. (E) Goodpasture syndrome presents with hemoptysis and/or hematuria, causing a nephritic syndrome. (F) Post-renal AKI is not as common as prerenal AKI or ATN, and can be ruled out with a renal ultrasound. (H) Fibromuscular dysplasia is most common in middle-aged women and is a cause of secondary hypertension. It may cause renal failure, but is not the most likely answer choice.

34

A 48-year-old woman presents to your clinic complaining of excessive urination and constant hunger and thirst. She has no other complaints and no past medical history. Her family history is significant for hypertension, type 2 diabetes mellitus, and hyperlipidemia. She does not smoke but lives a sedentary lifestyle. On examination, she is afebrile with a blood pressure of 134/88 mmHg, heart rate of 84 beats per minute, and respiratory rate of 14 breaths per minute. The rest of her examination is normal. The patient is scheduled for a return visit to have fasting laboratory tests drawn. At her return visit, her blood pressure is 138/86 mmHg. Her fasting glucose is 156 mg/dL, and urine albumin-to-creatinine ratio is 200 mg/g.

What is the next step in management for this patient?

- (A) Encourage diet and lifestyle modifications
- (B) Admit the patient to the hospital for aggressive glucose control and diabetes education
- (C) Start an ACE inhibitor now
- (D) Start hydrochlorothiazide now, and add an ACE inhibitor if this fails to achieve the target blood pressure

**The answer is C: Start an ACE inhibitor now.** This patient is presenting with a new diagnosis of diabetes mellitus and is normotensive; however, she has moderate albuminuria. Although there is debate over whether ACE inhibitors (or ARBs) should be used as primary prevention for diabetic nephropathy, there is good data to support starting an ACE inhibitor with at least moderate albuminuria (early diabetic nephropathy). It can be started whether or not the patient is hypertensive. The reason ACE inhibitors are thought to be renoprotective comes from their role in reducing intraglomerular pressure. Early in the course of diabetes, there is hyperfiltration and intraglomerular hypertension that damages the nephrons. ACE inhibitors and ARBs prevent angiotensin II from causing vasoconstriction of the efferent arterioles. The effect is relaxation of the efferent arteriole and a reduction in the intraglomerular pressure, which decreases proteinuria (which is itself toxic to the tubules) and delays the onset of diabetic nephropathy. The bottom line for the shelf examination is that ACE

inhibitors and ARBs are renoprotective in diabetes, and should be taken in nearly all diabetic patients with hypertension, nephropathy, and/or cardiovascular disease, whether or not they are hypertensive.

(A) Encouraging diet and lifestyle modifications is always a *right* answer, but is not always the *best* answer. In this case, it would be inappropriate to counsel the patient without starting an ACE inhibitor. (B) The patient is stable and can be managed as an outpatient. If the patient had diabetic ketoacidosis or hyperosmolar hyperglycemic state, then she should be managed as an inpatient. (D) The Eighth Joint National Committee (JNC 8) recommended a blood pressure target of <140/90 mmHg in all diabetic patients, and so an antihypertensive agent without renoprotective effects (e.g., hydrochlorothiazide) should not be started. (Note: remember that the shelf examination is not always up to date and might recommend a blood pressure goal of <130 to 135/80 to 85 mmHg.)

35

A 28-year-old woman with Crohn disease presents to the Emergency Department with back pain that started last night. She describes a colicky pain that is located on the right side of her back and shoots down to her groin. The pain is also associated with nausea and vomiting. Her temperature is 37.3°C, blood pressure is 128/84 mmHg, heart rate is 98 beats per minute, and respiratory rate is 18 breaths per minute. The patient appears uncomfortable and has some right flank pain on palpation. A pelvic examination is performed and shows no cervical discharge or cervical motion tenderness. Her laboratory values show a normal hemoglobin and leukocyte count, a urine pregnancy test is negative, and a urine dipstick shows 2+ blood but is negative for nitrites or leukocyte esterase.

What is the most likely diagnosis?

- (A) Pyelonephritis
- (B) Nephrolithiasis
- (C) Appendicitis
- (D) Ectopic pregnancy

**The answer is B: Nephrolithiasis.** This patient is presenting with the typical symptoms of a kidney stone. Patients with Crohn disease are at risk of developing calcium oxalate stones due to increased absorption of oxalate in the GI tract (and therefore increased oxaluria), which has two causes. First, malabsorption of bile salts and GI tract inflammation increase mucosal permeability. Second, fatty acids (also a result of malabsorption) bind intestinal calcium, and so less calcium is available to bind and trap intestinal oxalate. This causes an increase in free oxalate that can be absorbed, eventually making it back to the kidneys to be excreted.

Calcium stones are the most common type of kidney stones, and patients with these stones are encouraged to increase their dietary intake of calcium

(in order to decrease oxalate absorption in the GI tract). Thiazide diuretics may also be beneficial since they increase calcium reabsorption and therefore decrease urine calcium. Ammonium magnesium phosphate (struvite) stones are caused by urinary tract infections with urease-positive organisms (e.g., *Proteus*, *Klebsiella*) and can form staghorn calculi. Uric acid stones are associated with hyperuricemia (e.g., leukemia, gout). Cystine stones are seen in the genetic disease cystinuria and are treated by alkalinizing the urine with acetazolamide.

(A) Pyelonephritis would also produce flank pain, but unlike nephrolithiasis it would also produce fever, leukocytosis, and a urine dipstick showing infection (e.g., positive nitrites, positive leukocyte esterase). (C) Appendicitis is important to consider in any young patient with abdominal pain; however, it would be unusual for appendicitis to cause hematuria. (D) Ectopic pregnancies can mimic the pain of a kidney stone; however, this diagnosis is unlikely given the negative pregnancy test.

36

A 62-year-old woman with a long history of COPD presents to her physician for routine laboratory tests. She is currently healthy without any recent illnesses or changes in medications. Her laboratory values show a serum bicarbonate level of 36 mEq/L.

Which of the following best represents the natural compensatory response to this patient's acid/base disorder?

- (A) Increased reabsorption of  $\text{HCO}_3$  in the nephron
- (B) Decreased reabsorption of  $\text{HCO}_3$  in the nephron
- (C) Increased respiratory rate and/or tidal volume
- (D) Decreased respiratory rate and/or tidal volume
- (E) Increased  $\text{HCO}_3$  absorption in the GI tract

**The answer is A: Increased reabsorption of  $\text{HCO}_3$  in the nephron.** An elevated  $\text{HCO}_3$  is consistent with either a metabolic alkalosis or a respiratory acidosis. In this case, the presence of a chronic lung disease like COPD makes the likely diagnosis chronic respiratory acidosis. It is important to know the body's response to acid/base abnormalities (*Table 3-1*); however, the response will never completely correct the pH. If the pH is normal, then suspect a mixed acid/base disorder. The simplest way to view compensatory mechanisms is to think of renal compensations for respiratory problems and vice versa. For chronic respiratory acidosis, then, the compensation will be an increase in  $\text{HCO}_3$  reabsorption in the nephron (as well as an increase in the excretion of titratable acid and  $\text{NH}_4^+$ ). (B) Chronic respiratory alkalosis will have the opposite effect, with a decrease in  $\text{HCO}_3$  reabsorption. (C, D) In response to metabolic acidosis, the body will increase ventilation (respiratory rate  $\times$  tidal volume); in response to metabolic alkalosis, the body will decrease ventilation. If a metabolic acidosis persists, the body's kidneys will also increase the excretion of titratable acid and  $\text{NH}_4^+$ . (E) The GI tract is not a major contributor to acid/base homeostasis.

**37** A mother brings her 18-year-old son into the physician for a routine physical examination before starting college. He has no past medical history, does not take any medications, and denies any current symptoms. His vitals and physical examination are completely normal; however, a urine dipstick is positive for 1+ protein. A urine protein to creatinine ratio estimates that he is excreting 220 mg of protein per day. The patient has another urine sample collected 1 week later that shows persistent proteinuria.

Which of the following is the most likely cause of proteinuria in this patient?

- (A) Orthostatic proteinuria
- (B) Minimal change disease
- (C) Acute interstitial nephritis
- (D) Exercise-induced proteinuria

**The answer is A: Orthostatic proteinuria.** Orthostatic proteinuria is a very common condition in children and adolescents and has a benign course that usually resolves with time. It is the most common cause of isolated proteinuria in this age group and is diagnosed by comparing urine protein excretion while lying down (e.g., first morning void) and standing up. (B) Minimal change disease is the most common cause of nephrotic syndrome in children; however, glomerular disease is a less common cause of proteinuria in children and adolescents. There would be much higher levels of proteinuria in this condition and likely some physical manifestations (e.g., periorbital edema). (C) AIN would be suggested by intrinsic AKI, WBCs or WBC casts in the urine, and urine eosinophils. (D) Fever, exercise, and dehydration are some of the causes of *transient* proteinuria, which is also very common in this age group and resolves after the causative factor is removed. However, this patient has *persistent* proteinuria.

**38** A 62-year-old man with a history of hypertension, well-controlled diabetes, and coronary artery disease presents with shortness of breath. A history is obtained, with pertinent positives including orthopnea and leg swelling. His blood pressure is 146/94 mmHg with a heart rate of 84 beats per minute. The patient has an S3 on cardiac auscultation, bilateral rales are heard along the lung bases, and there is pitting edema around the ankles. Laboratory tests are ordered, which show a creatinine of 2.4 mg/dL (baseline 1.0 mg/dL).

What is the next step in managing this patient's renal failure?

- (A) IV fluids
- (B) Give ketorolac to increase the GFR
- (C) Systemic corticosteroids
- (D) IV furosemide

**The answer is D: IV furosemide.** The most important treatment of AKI is managing the underlying condition, which in this case is heart failure. The patient has a suggestive history and physical examination of CHF, and he is fluid overloaded. It might be surprising that prerenal AKI (caused by decreased blood flow to the kidneys) could occur in the setting of hypervolemia. However, even though the patient has ample blood volume, the *effective arterial volume* is decreased due to heart failure and poor cardiac output (i.e., large blood volume but poor flow). Therefore the kidneys are receiving less blood flow and responding the same way as they would in the setting of hypovolemia. Diuresis with IV furosemide would correct the patient's volume overload, allowing the heart's function to improve and increase blood flow to the kidneys. This is often called cardio-renal syndrome.

(A) Although IV fluids are used to treat prerenal AKI caused by hypovolemia, in this case it would worsen the AKI because it would further exacerbate his heart failure. (B) Starting an NSAID would decrease the GFR further due to afferent arteriole vasoconstriction, worsening the patient's prerenal AKI and potentially precipitating ATN. (C) Corticosteroids may be used in AIN if the kidneys fail to respond to the withdrawal of the offending agent, although there is mixed evidence as to the efficacy.



39 An older man is admitted to the hospital with weakness and palpitations. An ECG is performed and shown below (Figure 3-7).

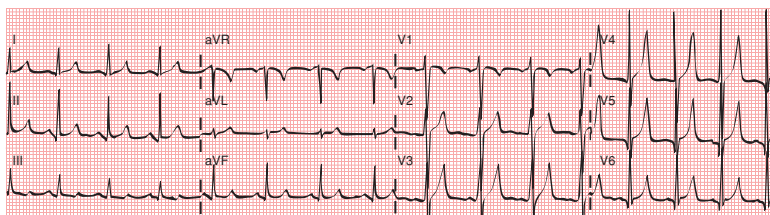


Figure 3-7

Which of the following is NOT a cause of this electrolyte abnormality?

- (A) Excessive insulin administration
- (B) Metabolic acidosis
- (C) Ischemic bowel
- (D) Excessive  $\beta$ -blocker administration
- (E) Excessive ACE inhibitor administration

**The answer is A: Excessive insulin administration.** It is important to recognize the classic ECG changes in hyperkalemia, which are peaked T waves, an increased PR interval, and an increased QRS width. If left untreated, the

QRS complexes will progress to a sine wave pattern. All of the following will increase serum potassium concentrations: **(D, E)** anything that decreases the activity of the sodium–potassium ATPase (e.g.,  $\beta$ -blockers, digoxin, ACE inhibitors/ARBs and hypoaldosteronism, insulin *deficiency*); **(B)** anything that causes acidemia and a transcellular shift of hydrogen ions into cells and potassium ions out of cells; **(C)** anything causing massive cell death/lysis (e.g., ischemic bowel, hemolysis, rhabdomyolysis, tumor lysis syndrome); and anything causing renal disease or a decrease in effective arterial volume (e.g., CHF, liver failure) that leads to the inability to excrete potassium. Also, be aware of pseudohyperkalemia, in which the laboratory sample that was drawn undergoes hemolysis and gives a falsely high serum potassium value.

40

A 41-year-old woman is placed on enalapril to treat her hypertension. She has no significant medical history and is otherwise healthy. She has her laboratory samples drawn 5 days later, which show a serum potassium of 4.2 mEq/L, a BUN of 13 mg/dL, and a creatinine of 1.1 mg/dL (baseline 0.9 mg/dL). A urinalysis is normal.

What should be done next in the management of this patient?

- (A)** Continue the current medication
- (B)** Discontinue enalapril and start hydrochlorothiazide
- (C)** Discontinue enalapril and start losartan
- (D)** Add hydrochlorothiazide
- (E)** Add ibuprofen to normalize the GFR

**The answer is A: Continue the current medication.** A modest decrease in the GFR may occur in as little as a few days after starting an ACE inhibitor. Up to a 30% increase in creatinine from baseline is tolerable, and the medication does not need to be discontinued. **(B)** This patient is otherwise healthy with a normal urinalysis, and therefore enalapril may be continued for now with periodic monitoring. **(C)** ARBs may produce a similar mild reduction in GFR, and so it would not make sense to switch medications. **(D)** Adding another antihypertensive should be done if the patient's blood pressure fails to respond to an appropriate dose of the first drug. **(E)** NSAIDs would reduce the GFR further, and therefore the combination of an ACE inhibitor and an NSAID places the patient at risk of renal ischemia.



## Gastroenterology

1

A 36-year-old man presents with cramping abdominal pain, urgency, bloody diarrhea, and weight loss. Physical examination reveals low-grade fever, heme positive stools, and tenderness to palpation in the lower abdomen. Colonoscopy with biopsy is performed and the diagnosis of Crohn disease is made.

Which of the following findings is not associated with Crohn disease?

- (A) Loss of haustral markings (lead-pipe colon)
- (B) Transmural inflammation
- (C) Oral ulcers
- (D) Noncaseating granulomas on biopsy
- (E) Perirectal fistulas

**The answer is A: Loss of haustral markings (lead-pipe colon).** Distinguishing the two types of inflammatory bowel disease (IBD), Crohn disease and ulcerative colitis, is crucial to performing well on the gastroenterology questions on the medicine shelf examination. It is very difficult to determine the diagnosis simply from symptoms, although ulcerative colitis is more likely to be associated with bloody diarrhea and “cramping” abdominal pain, as opposed to the “colicky” pain often seen in Crohn’s. Given the nonspecific symptoms of IBD, a colonoscopy with biopsy is crucial to making the correct diagnosis. **(B, C, D, E)** Crohn disease is a chronic inflammatory bowel disease involving *transmural* (affecting the entire bowel wall) inflammation that can occur anywhere from the mouth to the anus (skip lesions). Crohn’s patients can present not only with lesions in the colon but also with lesions in the small bowel and even oral ulcers. Extraintestinal manifestations are common in Crohn disease as well, and include perirectal abscesses and fistulas. Biopsy in Crohn disease reveals noncaseating granulomas with mononuclear cell infiltrate. Ulcerative colitis, on the other hand, is associated with friable mucosa with ulcerations and erosions on colonoscopy; barium enema often reveals a

lead-pipe colon with loss of haustra. Biopsy in ulcerative colitis reveals crypt abscesses and microulcerations (but no granulomas).

2

A 29-year-old woman presents to the physician because of fatigue, dark urine, nausea, vomiting, and decreased appetite. She reports that the symptoms started 1 month ago and have worsened in the last week. She has an insignificant past medical history but does endorse IV drug use as well as unprotected sexual intercourse with several partners over the last 6 months. She is unable to recall her immunization history. Laboratory results show elevated AST (210 U/L) and ALT (352 U/L) levels. The physician determines she is at high risk for hepatitis B virus.

What laboratory test(s) should be ordered to screen for ACUTE hepatitis B infection?

- (A) Anti-HBe
- (B) HBsAg and anti-HBs
- (C) HBeAg
- (D) HBsAg and IgM anti-HBc

**The answer is D: HBsAg and IgM anti-HBc.** Testing for HBsAg and IgM anti-HBc is the best screening test for acute hepatitis B infection. HBsAg is the first marker detected in the blood after exposure and actually occurs before elevation in AST/ALT levels or clinical symptoms. HBsAg can be detected throughout the symptomatic phase of acute hepatitis B infection and its presence is indicative of infectivity. Anti-HBc appears shortly after HBsAg appears and the IgM component indicates the acute phase of the disease, whereas the IgG component indicates recovery from the disease. The period between the disappearance of HBsAg and the appearance of anti-HBs is called the “window period.” IgM anti-HBc is present during the “window period” when anti-HBs is not yet detectable and thus is used as a marker for the diagnosis of acute hepatitis. (A, B, C) HBeAg appears soon after HBsAg appears and indicates active viral replication and very high infectivity. It is followed by anti-HBe, and its presence for more than 3 months signifies an increased probability of chronic hepatitis B. Anti-HBs is present in individuals who have been vaccinated or have cleared HBsAg; thus it is present for life.

3

A 39-year-old woman presents with epigastric pain that has radiated to her back for the last 8 hours. She endorses nausea and vomiting. Her past medical history is significant for hyperlipidemia; however, she does not take any medications other than a multivitamin. She denies alcohol or drug use. On examination, the patient is slightly febrile at 38.4°C, with a blood pressure of 114/83 mmHg, a heart

rate of 98 beats per minute, and a respiratory rate of 22 breaths per minute. The patient has decreased bowel sounds and guarding in the midepigastrium.

Which of the following results is the most specific finding in this condition?

- (A) Elevated amylase
- (B) Elevated ALT
- (C) Elevated lipase
- (D) Positive fecal fat test

**The answer is C: Elevated lipase.** The patient in this question is presenting with signs and symptoms of acute pancreatitis (epigastric abdominal pain radiating to the back, nausea, and vomiting). The vast majority of cases (80%) result from gallstones and alcohol. However, other causes of acute pancreatitis can be remembered with the mnemonic *GET SMASHED* (Gallstones, Ethanol, Trauma, Steroids, Mumps, Autoimmune, Scorpion bite, Hyperlipidemia, ERCP, Drugs [specifically diuretics, gliptins, azathioprine, salicylates, steroids]).

Acute pancreatitis can be diagnosed through several modalities: physical examination demonstrating epigastric pain radiating to the back, elevated amylase and lipase levels (typically  $3\times$  higher than the normal limit), and abdominal imaging (CT) showing pancreatic enlargement with heterogeneous enhancement with IV contrast. Ultrasound is also helpful in diagnosing gallstone pancreatitis by visualizing gallstones in the gallbladder. Lipase has the greatest *specificity* of all possible tests and is usually more elevated than amylase in acute pancreatitis.

(A) Amylase can sometimes be normal in acute pancreatitis (particularly if the etiology is hyperlipidemia). Furthermore, amylase is not specific to the pancreas as there is not only pancreatic amylase but also salivary amylase. (B) Although elevated ALT is very useful in suggesting *gallstone* pancreatitis, it does not encompass all the causes of acute pancreatitis and therefore is not a specific test. (D) Positive fecal fat test is typically positive ( $>7$  g/d) in *chronic* pancreatitis; however, chronic pancreatitis presents with symptoms of malabsorption (as opposed to pain) and is typically due to alcohol use (neither of which this patient endorses).



A 49-year-old man with an extensive history of intravenous drug abuse over 10 years ago presents with anorexia, nausea, and malaise. He also reports dark urine for the last 2 months. His past medical history is significant for bipolar type 2 disorder. He takes no medications and reports a distant history of alcohol abuse. Physical examination is significant for hepatomegaly but no ascites. The patient demonstrates no signs of depression. Laboratory results reveal the following.

|                                      |                                        |
|--------------------------------------|----------------------------------------|
| Albumin                              | 3.6 g/dL                               |
| Total bilirubin                      | 1.2 mg/dL                              |
| Direct bilirubin                     | 0.8 mg/dL                              |
| Aspartate aminotransferase           | 420 U/L                                |
| Alanine aminotransferase             | 280 U/L                                |
| Alkaline phosphatase                 | 78 U/L                                 |
| Prothrombin time (PT)                | 12 s                                   |
| International normalized ratio (INR) | 1.3                                    |
| Hemoglobin                           | 12.8 mg/dL                             |
| Creatinine                           | 1.2 mg/dL                              |
| Polymerase chain reaction            | Detectable serum hepatitis C virus RNA |

A biopsy of the liver is performed that demonstrates bridging fibrosis.

Which of the following is the best next step in management of this patient?

- (A) Follow-up in 4 months with monitoring of symptoms
- (B) Vaccinate him against hepatitis B virus (HBV) and Hepatitis A virus (HAV)
- (C) Upper endoscopy
- (D) Liver transplantation

**The answer is B: Vaccinate him against hepatitis B virus (HBV) and Hepatitis A virus (HAV).** The patient in this question has chronic hepatitis C virus (HCV) infection. Deciding to treat HCV depends on a variety of factors. Criteria for treatment that is considered “widely accepted” include patient age >18 years, liver biopsy demonstrating chronic hepatitis with bridging fibrosis, detectable serum HCV RNA, *compensated* liver disease (INR <1.5 without ascites), and stable laboratory findings such as creatinine and hemoglobin. Of note, *contraindications* to treatment include active and ongoing alcohol or drug abuse and uncontrolled depression, neither of which our patient demonstrates. Therefore, the decision to treat here is the best next step. Although the current gold standard HCV treatment is combination therapy with interferon and ribavirin, this is currently changing as research progresses to find more interferon-free regimens. However, regardless of the aforementioned criteria, the patient must be vaccinated against HBV and HAV. (A) Close observation is not the best step

here as our patient meets all the criteria for treatment. (C) Upper endoscopy would be useful in a patient with cirrhosis who shows signs of portal hypertension (which our patient does not demonstrate). (D) Liver transplantation should only be considered in *decompensated* liver failure; however, our patient demonstrates normal INR and normal serum albumin levels.

5

A 27-year-old woman presents with diarrhea and abdominal pain for the last 8 months. She denies bloody stools, weight loss, or fatigue. The patient just recently started what she describes as a “stressful” career in investment banking. She is concerned that she might have Crohn disease as both her maternal uncle and maternal grandmother have the disorder. Further questioning reveals that the diarrhea and abdominal pain occur about once per week (generally Friday mornings before she gives her weekly presentation), and the other days she is “constipated.” The abdominal pain is alleviated after defecation. Physical examination is unremarkable.

What is the next best step in management for this patient?

- (A) Colonoscopy
- (B) Oral corticosteroids
- (C) Loperamide
- (D) Reassurance and recommendation for a high-fiber diet and exercise

**The answer is D: Reassurance and recommendation for a high-fiber diet and exercise.** This is a very common question on the Internal Medicine shelf examination. The patient in this question likely has irritable bowel syndrome (IBS) given that she endorses abdominal pain with altered bowel function (diarrhea and constipation), with complete relief of abdominal pain after defecation. The etiology of IBS is largely unknown, but may be related to psychological factors, autonomic nervous system abnormalities, and altered gut motor function. The patient should be reassured that this is not inflammatory bowel disease (IBD) given that she does not have cramping, bloody diarrhea, or systemic symptoms like weight loss or fatigue. Nonetheless, a high-fiber diet (30 g/d) should be emphasized as well as exercise and sufficient fluid intake. (C) Loperamide is an opioid-receptor agonist used in the treatment of diarrhea. This should only be considered in IBS if the diarrhea persists after the aforementioned recommendations are tried. (A) Colonoscopy can aid in diagnosing IBD (Crohn disease shows skip lesions and ulcerative colitis shows friable mucosa with ulcerations and erosions continuous from the anus). (B) Corticosteroids are used in the treatment of IBD.

6

A 36-year-old man presents to the physician with fatigue and “brown” urine. He has an unremarkable past medical history and endorses IV drug use in his early 20s. Family history is significant for breast cancer

on his mother's side and rheumatoid arthritis on his father's side. He is afebrile, has a blood pressure of 132/72 mmHg, and a heart rate of 84 beats per minute. Physical examination reveals icteric sclera and skin and pain in the right upper quadrant to deep palpation. Laboratory results reveal the following.

|                                   |           |
|-----------------------------------|-----------|
| Total protein                     | 6.0 g/dL  |
| Albumin                           | 3.6 g/dL  |
| Total bilirubin                   | 9.8 mg/dL |
| Direct bilirubin                  | 7.9 mg/dL |
| Aspartate aminotransferase        | 19 U/L    |
| Alanine aminotransferase          | 20 U/L    |
| Alkaline phosphatase              | 760 U/L   |
| Amylase                           | 42 U/L    |
| Prothrombin time (PT)             | 12 s      |
| Partial thromboplastin time (PTT) | 32 s      |

Which of the following is the best next step in the diagnostic workup?

- (A) Viral hepatitis panel
- (B) Endoscopic retrograde cholangiopancreatogram (ERCP)
- (C) Abdominal ultrasonography
- (D) Liver biopsy

**The answer is C: Abdominal ultrasonography.** The patient in this question is presenting with conjugated hyperbilirubinemia. If he had presented with a high indirect bilirubin, this would be a mainly unconjugated hyperbilirubinemia (possible causes include hemolysis and a conjugation defect like Gilbert's). He also presents with a nonspecific slightly increased AST and ALT and a highly increased alkaline phosphatase level (760 U/L). In this setting, elevated alkaline phosphatase signifies cholestasis with biliary obstruction. The best next step in this clinical scenario is to order an abdominal ultrasound to determine whether the cholestasis is extrahepatic (biliary dilatation) or intrahepatic (no sign of biliary dilatation). (A) Viral hepatitis, acute type, is typically associated with highly elevated AST and ALT levels; however, this patient has normal levels and likely does not have a viral hepatitis.

Nonetheless, it should be noted that chronic viral hepatitis that has led to cirrhosis could actually have mildly elevated, and even normal, levels of liver enzymes. This patient has normal albumin and coagulation studies, however, and therefore does not likely have cirrhosis. **(B)** ERCP is a procedure that can be both diagnostic and therapeutic by relieving obstruction and allowing for biliary drainage. Nonetheless, imaging must be performed first to determine the presence of obstruction before ERCP is considered. **(D)** Liver biopsy is not indicated at this time without radiologic clues to the underlying diagnosis.

7

A 28-year-old man presents with fatigue and cognitive deterioration. He reports that in the last 2 months he has forgotten several of his friends' names. His girlfriend states that he has been "impulsive" and has made several poor decisions such as urinating in public and cursing (which he has never done before). Physical examination reveals non-specific abdominal pain to deep palpation in the right upper quadrant in addition to the finding seen in the photo below (*Figure 4-1*).



**Figure 4-1**

Which of the following laboratory findings do you expect with this condition?

- (A)** Elevated ferritin
- (B)** Decreased serum ceruloplasmin
- (C)** Decreased urinary copper
- (D)** Elevated serum copper

**The answer is B: Decreased serum ceruloplasmin.** The patient in this question is presenting with neuropsychiatric symptoms and the physical examination finding of Kayser-Fleischer rings (copper deposition in a ring around the cornea) consistent with a diagnosis of Wilson disease. Wilson disease is an autosomal recessive disorder in which copper accumulates in tissues due to mutations

in the Wilson disease protein (ATP7B) gene; this causes a defect in incorporation of copper in hepatic lysosomes. The main sites of copper accumulation are the liver and the brain. Kayser–Fleischer rings are pathognomonic for the condition and result from copper deposition in Descemet membrane (the basement membrane between the stroma and the endothelial layer of the cornea).

The faulty incorporation of copper in the liver leads to defective synthesis of ceruloplasmin, a protein carrier of copper. The resulting high unbound copper in the serum causes deposits in the cornea, liver, and several neurologic structures (basal ganglia, brainstem, cerebral cortex, etc.). (C, D) The diagnosis of Wilson disease is based on laboratory findings: high urinary copper, low serum ceruloplasmin, low serum copper (the low ceruloplasmin causes the bound portion of copper to be low), and high hepatic copper content on liver biopsy. Treatment is with chelation with penicillamine. (A) Elevated ferritin is associated with hereditary hemochromatosis, an autosomal recessive disorder of iron overload (not copper).



A 47-year-old woman presents to the physician with fatigue, pruritus, and jaundice. Physical examination demonstrates xanthelasma, hepatosplenomegaly, and jaundice. Laboratory findings reveal elevated alkaline phosphatase and total bilirubin in addition to the presence of anti-mitochondrial antibody (AMA) and antinuclear antibody (ANA). Liver biopsy demonstrates inflammation of the bile ducts with intraepithelial lymphocytes.

What is the most likely diagnosis?

- (A) Autoimmune hepatitis
- (B) Primary sclerosing cholangitis
- (C) Primary biliary cirrhosis
- (D)  $\alpha_1$ -antitrypsin deficiency

**The answer is C: Primary biliary cirrhosis.** The patient in this question is demonstrating signs, symptoms, and laboratory findings consistent with a diagnosis of primary biliary cirrhosis, a disease involving autoimmune destruction of intrahepatic bile ducts. The disease commonly affects women and presents with fatigue, pruritus, jaundice, and sometimes fat malabsorption. Diagnosis is suggested by a highly elevated alkaline phosphatase and total bilirubin, but the most specific finding is the presence of *anti-mitochondrial antibodies*. Liver biopsy is performed to confirm the diagnosis and determine the stage of the disease. Treatment involves minimizing the associated cholestasis with ursodeoxycholic acid. (A) Autoimmune hepatitis is associated with antismooth muscle antibody. (B) Primary sclerosing cholangitis is often seen in inflammatory bowel disease and is associated with p-ANCA antibodies. (D)  $\alpha_1$ -antitrypsin deficiency usually affects both the liver and the lungs and is diagnosed by the absence of  $\alpha_1$ -antitrypsin on serum protein electrophoresis (SPEP).



9

A 33-year-old man presents with diarrhea for the last 6 weeks. He reports that his stools float and have an oily appearance. They have also been particularly foul smelling. He also endorses a nonspecific and diffuse abdominal pain as well as a 2.3-kg (5-lb) weight loss during this time period. Physical examination is unremarkable and laboratory results reveal a mild iron deficiency anemia. Antibody assays are positive for antiendomysial antibody.

Which of the following is the recommended treatment for this condition?

- (A) Treatment with corticosteroids
- (B) Treatment with metronidazole
- (C) Gluten-free diet
- (D) Treatment with loperamide

**The answer is C: Gluten-free diet.** The patient in this question is presenting with several nonspecific symptoms (abdominal pain, weight loss, chronic diarrhea) as well as iron deficiency anemia that are consistent with a diagnosis of celiac sprue (celiac disease). The presence of antiendomysial antibody suggests the diagnosis; however, tissue biopsy is still considered the gold standard in the diagnosis of celiac sprue. Tissue biopsy will demonstrate flattening or villous atrophy and inflammation. The only effective treatment is a lifelong gluten-free diet. Gluten is present in most grains in the Western world including wheat, barley, several additives, and processed foods, so patients should receive dietary counseling to ensure compliance with the gluten-free diet. (A) In the case of refractory disease in which alternative causes have been ruled out, corticosteroids may be considered. (B) Although the patient in this question presents with chronic diarrhea (>4 weeks), his other clinical symptoms and positive antiendomysial antibody make the diagnosis of *Clostridium difficile* unlikely. Therefore, treatment with metronidazole is not indicated. (D) Although loperamide will improve the diarrhea, it does not treat the underlying cause of the patient's constellation of symptoms, which is celiac sprue.

10

A 44-year-old man with a recent diagnosis of diabetes mellitus type 2 presents with joint pain, fatigue, and jaundice. He reports that his wife has noted that he looks "tanner" than usual. Physical examination demonstrates clubbing of the fingers, splenomegaly, and gynecomastia. Laboratory results reveal mildly increased AST and ALT, as well as an increased transferrin saturation (72%) and an increased ferritin level (410 ng/mL).

Which of the following is the recommended treatment for this condition?

- (A) N-acetylcysteine
- (B) Penicillamine
- (C) Ursodeoxycholic acid and fat-soluble vitamins
- (D) Periodic phlebotomies

**The answer is D: Periodic phlebotomies.** The patient in this question is presenting with the classic triad of cirrhosis, bronze skin, and diabetes consistent with a diagnosis of hereditary hemochromatosis. Hereditary hemochromatosis is an autosomal recessive disorder of iron overload and typically affects middle-aged Caucasian men. Patients usually present with a mild transaminitis, diabetes mellitus, arthritis, infertility, and sometimes heart failure. Transferrin saturation is commonly used as a screening test for hereditary hemochromatosis and will be elevated. Other laboratory values include increased ferritin levels and increased iron saturation. If suspicious of the diagnosis, the presence of the HFE gene mutation can serve as diagnostic confirmation. Treatment includes periodic phlebotomies to decrease the iron load. These are usually scheduled at weekly intervals until ferritin levels are within the normal range. If phlebotomy treatment is not feasible for the patient, long-term administration of an iron-chelating compound such as deferoxamine is helpful. (A) *N*-acetylcysteine is used in the treatment of acetaminophen toxicity. (B) Penicillamine is a copper chelator used in the treatment of Wilson disease. (C) Ursodeoxycholic acid reduces cholesterol absorption and is used to dissolve gallstones; it is also used in the treatment of primary biliary cirrhosis and primary sclerosing cholangitis.



A 53-year-old man with a history of peptic ulcer disease and hypertension presents with hematemesis. A nasogastric tube is placed and a large amount of coffee ground material is lavaged. The patient has a temperature of 37°C, blood pressure of 88/42 mmHg, heart rate of 112 beats per minute, respiratory rate of 20 breaths per minute, and oxygen saturation of 97% on room air. Physical examination reveals delayed capillary refill.

Which of the following is the best next step in management of this patient?

- (A) Immediate upper GI endoscopy
- (B) Administration of fluids
- (C) *H. pylori* serologic testing
- (D) Intravenous (IV) proton pump inhibitor

**The answer is B: Administration of fluids.** This is a common question on the Internal Medicine shelf examination that emphasizes the importance of airway, breathing, and circulation (ABCs) in the management of patients (regardless of the underlying disorder). This patient presents with hypotension and delayed capillary refill, indicating that there is compromise of his circulation. The best next step in management of circulatory compromise (in this case from an upper GI bleed) is fluid resuscitation. After the patient is hemodynamically stable, treatment for the actual underlying condition can be initiated. (A, C, D) All these answer choices address the underlying cause of the upper GI bleeding (likely peptic ulcer bleeding); however, the patient must be stabilized before these modalities are pursued.

12

A 57-year-old woman with a history of hypertension and diabetes mellitus type 2 presents with dysphagia to both solids and liquids. She reports that starting 5 months ago she had difficulty swallowing solids only, but it has progressed to difficulty swallowing liquids as well. She endorses a 5.44-kg (12-lb) weight loss as well as heartburn during this time frame. Physical examination is unremarkable. A barium swallow study is ordered (*Figure 4-2*) and manometry confirms the diagnosis.



**Figure 4-2**

Which of the following is the best next step in management of this patient?

- (A) Surgical myotomy
- (B) Amlodipine
- (C) Endoscopic evaluation
- (D) Pantoprazole

**The answer is C: Endoscopic evaluation.** The patient in this question is presenting with signs and symptoms (dysphagia to solids and liquids, weight loss, heartburn) consistent with a diagnosis of achalasia, which is an esophageal motility disorder involving the smooth muscle layer of the esophagus and the LES. If there is dysphagia to both solids and liquids, then it is likely a motility problem whereas if the dysphagia started to solids and progressed to liquids, then it is likely mechanical obstruction. The result is a loss of peristalsis in the distal esophagus and loss of appropriate LES relaxation during swallowing. Although diagnosis is suspected clinically, a barium swallow is the first step in management and demonstrates a “bird-beak” at the gastroesophageal junction. Manometry will further confirm the diagnosis with elevated resting LES pressure and incomplete LES relaxation after swallowing. It is absolutely critical that esophageal cancer is ruled out first, though it can produce identical symptoms to achalasia (pseudoachalasia). Therefore, endoscopy must be performed to rule out esophageal cancer at the gastroesophageal junction before proceeding with treatment. (A) Good surgical candidates are generally recommended for surgical myotomy as the definitive treatment for achalasia. (B) Poor surgical candidates can proceed with medical therapy, such as calcium channel blockers and botulinum toxin injection. (D) A proton pump inhibitor might improve the patient’s heartburn, but will not resolve the dysphagia.



**13** A 49-year-old morbidly obese man with a 40 pack-year history of smoking presents with worsening heartburn. The patient reports that he has had heartburn for 3 years, but it has worsened over the past 3 months. Over-the-counter medications do not ameliorate his symptoms anymore. Upper endoscopy is performed and a hiatal hernia is diagnosed. The patient adamantly refuses any medical or surgical intervention.

Which of the following is he at risk for developing?

- (A) Squamous cell carcinoma (SCC) of the esophagus
- (B) Adenocarcinoma of the esophagus
- (C) Esophageal perforation
- (D) Mallory–Weiss tear

**The answer is B: Adenocarcinoma of the esophagus.** The patient in this question is presenting with signs and symptoms of gastroesophageal reflux disease (GERD). His chronic GERD is likely the result of the hiatal hernia. Chronic GERD causes the normal squamous epithelium in the lower end of the esophagus to be replaced with columnar epithelium (Barrett esophagus). Barrett esophagus is a major risk factor for developing esophageal cancer, specifically the adenocarcinoma type. (A) SCC of the esophagus tends to occur in the upper two-thirds of the esophagus with risk factors

including smoking, alcohol, hot food and beverages, vitamin deficiencies, and viral infections. Barrett esophagus is not a risk factor for SCC of the esophagus. (C) Esophageal perforation is typically iatrogenic, usually due to medical instrumentation. (D) Mallory–Weiss tears cause bleeding in the mucosa at the gastroesophageal junction and are usually caused by severe alcoholism and retching.

14

A 61-year-old man presents with abdominal pain, vomiting, jaundice, and a weight loss of 9.1 kg (20 lb) over the last 4 months. His abdominal pain is localized to the right upper quadrant and radiates to the back. The patient has a temperature of 37°C, blood pressure of 120/80 mmHg, heart rate of 106 beats per minute, and a respiratory rate of 22 breaths per minute. Physical examination reveals a 6-cm palpable mass below the right costal margin. Ultrasound confirms an enlarged gallbladder. Laboratory results reveal the following.

|                            |           |
|----------------------------|-----------|
| Albumin                    | 3.1 g/dL  |
| Total bilirubin            | 2.6 mg/dL |
| Direct bilirubin           | 1.9 mg/dL |
| Aspartate aminotransferase | 78 U/L    |
| Alanine aminotransferase   | 61 U/L    |
| Alkaline phosphatase       | 390 U/L   |
| Amylase                    | 210 U/L   |

Which of the following is the best next step in the diagnostic workup of this patient?

- (A) Abdominal CT scan
- (B) Laparoscopy with surgical biopsy
- (C) Endoscopic retrograde cholangiopancreatography (ERCP)
- (D) Abdominal x-ray

**The answer is A: Abdominal CT scan.** The patient in this question is presenting with an enlarged palpable gallbladder (Courvoisier sign) and signs, symptoms, and laboratory values consistent with biliary obstruction (elevated direct bilirubin, elevated alkaline phosphatase, and jaundice). These clinical and laboratory findings support the most likely diagnosis as pancreatic cancer (specifically carcinoma of the head of the pancreas). The best imaging modality with suspected pancreatic

carcinoma is the abdominal CT scan. (B) Laparoscopy is not indicated with pancreatic cancer. (C) ERCP might eventually be warranted, but is not the best initial test. (D) Abdominal films are helpful in patients with suspected cholelithiasis (gallstones) or to detect calcifications from chronic pancreatitis.

15

A 42-year-old woman presents with unrelenting abdominal pain for the past 2 days. The pain is epigastric in location and occasionally radiates to her back. She has vomited numerous times and cannot tolerate food or liquids. She has no significant past medical history, but does endorse drinking two bottles of wine per day for the last 5 years. She has a temperature of 37°C, blood pressure of 98/64 mmHg, heart rate of 110 beats per minute, and a respiratory rate of 20 breaths per minute. Physical examination reveals epigastric tenderness to deep palpation without guarding or rebound. Amylase and lipase levels are elevated more than four times that of the upper limit of normal.

Which of the following complications is NOT associated with this condition?

- (A) Pleural effusion
- (B) Ileus
- (C) Renal failure
- (D) Mesenteric ischemia

**The answer is D: Mesenteric ischemia.** The patient in this question is presenting with classical symptoms of acute pancreatitis (nausea, vomiting, epigastric pain radiating to the back), in addition to laboratory values consistent with acute pancreatitis (elevated amylase and lipase). Alcohol use and gallstones are the most common causes of acute pancreatitis (this patient endorses a history of alcoholism). This question tests the student's ability to recall the complications associated with acute pancreatitis. Complications typically seen with acute pancreatitis include pleural effusion, renal failure, ileus, and respiratory distress. Mesenteric ischemia is not associated with acute pancreatitis.

16

A 32-year-old man presents with several months of dysphagia to solid foods and a "sticky" feeling in his throat whenever he eats. In addition, he endorses chest pain when he drinks really hot beverages; however, he says that it is transient in nature, only occurs for a few seconds, does not radiate, and then dissipates on its own. Past medical history is insignificant. Esophageal manometry reveals periodic, high-amplitude, nonperistaltic waves.

Which of the following is the likely diagnosis?

- (A) Achalasia
- (B) Scleroderma
- (C) Diffuse esophageal spasm
- (D) Peptic ulcer disease

**The answer is C: Diffuse esophageal spasm.** The patient in this question is presenting with chest pain and dysphagia without heartburn. Given the manometry findings of periodic, high-amplitude, nonperistaltic waves, the diagnosis is likely diffuse esophageal spasm. In this condition, the spasms do not propel food effectively to the stomach due to uncoordinated contractions. The cause is unknown; however, many cases seem to result from uncontrolled GERD. It is thought that very cold and hot beverages trigger a spasm. Treatment includes nitroglycerin and calcium channel blockers. (A) Achalasia would have an increased lower esophageal sphincter (LES) tone. (B) Scleroderma is associated with absence of peristaltic waves in the lower two-thirds of the esophagus and a decreased LES tone. (D) Peptic ulcer disease is not associated with dysphagia.



A 61-year-old man with a history of hypertension and congestive heart failure presents with abdominal “bloating” for the last 9 months. He also endorses significant swelling of his feet and timidly mentions that his chest is starting to “resemble that of a female.” He denies alcohol or drug use. Physical examination reveals abdominal ascites, bilateral gynecomastia, and spider angiomas on his torso.

Which of the following is likely the cause of his underlying disorder?

- (A) Drug toxicity
- (B) Malignancy
- (C) Autoimmune disorder
- (D) Viral infection

**The answer is D: Viral infection.** The patient in this question is presenting with signs of chronic liver disease consistent with a diagnosis of cirrhosis. Other symptoms include pedal edema, palmar erythema, caput medusa (*Figure 4-3*), splenomegaly, testicular atrophy, and nail changes. The most common causes of cirrhosis are alcohol abuse (which the patient denies) and viral hepatitis (specifically hepatitis B or C). (A) Drug toxicity can cause acute liver failure, which causes rapid development of hepatocellular dysfunction. Specifically, coagulopathy and mental status changes (encephalopathy) in a patient without known prior liver disease are seen. (B) Although cirrhotic patients are at an increased risk for developing hepatocellular carcinoma (HCC), the converse does not hold true. (C) Autoimmune conditions are less common causes of cirrhosis.



**Figure 4-3**

**18** A 41-year-old woman with a history of diabetes mellitus type 2 presents with a 2-month history of abdominal pain. She reports upper abdominal pain and nausea that is worse 30 to 45 minutes after eating a meal. She denies vomiting, diarrhea, or weight loss. Physical examination including vital signs is unremarkable. Laboratory studies reveal the following.

|                            |           |
|----------------------------|-----------|
| Albumin                    | 3.7 g/dL  |
| Total bilirubin            | 0.7 mg/dL |
| Aspartate aminotransferase | 22 U/L    |
| Alanine aminotransferase   | 21 U/L    |
| Alkaline phosphatase       | 71 U/L    |
| Hemoglobin                 | 13.1 g/dL |



Which of the following is the best next step in management of this patient?

- (A) Antacids
- (B) Barium swallow evaluation
- (C) Empiric 1-month trial with proton pump inhibitor (PPI)
- (D) Upper GI endoscopy

**The answer is C: Empiric 1-month trial with proton pump inhibitor (PPI).** The patient in this question is presenting with dyspepsia (characterized by epigastric pain and early satiety). Dyspepsia is a common presentation, and only a minority of patients is diagnosed with an underlying etiology contributing to the dyspepsia. The most common etiologies of dyspepsia are GERD, NSAIDs, peptic ulcer disease, and malignancy. (D) Importantly, if a patient presents with any “alarm symptoms” such as unexplained weight loss, persistent vomiting, blood loss, dysphagia, or family history of gastrointestinal cancer, then he/she should undergo an upper GI endoscopy to evaluate for malignancy. In patients without the “alarm symptoms,” current recommendations are to test for *H. pylori* in regions where there is a high prevalence of the bacteria and begin treatment with a proton pump inhibitor (PPI). In regions where there is a low prevalence of *H. pylori*, some physicians will treat empirically with a PPI. The most important thing to note here is that patients who fail either of these treatment options after 4 to 8 weeks should undergo endoscopy. (A, B) Antacids and barium swallow evaluations are not helpful in treating peptic ulcer disease.

19

A 21-year-old woman presents with a slight yellowing of her skin that her boyfriend noticed yesterday. She feels well and has no other complaints. Her past medical history is unremarkable, but she does report that she has not been eating enough recently due to stress from her upcoming college final examinations. Physical examination is significant only for mild jaundice of the skin. Laboratory results reveal the following.

|                            |           |
|----------------------------|-----------|
| Total bilirubin            | 3.1 mg/dL |
| Indirect bilirubin         | 2.9 mg/dL |
| Aspartate aminotransferase | 22 U/L    |
| Alanine aminotransferase   | 21 U/L    |
| Hemoglobin                 | 13.9 g/L  |

Which of the following is the most likely diagnosis?

- (A) G6PD deficiency
- (B) Gilbert syndrome
- (C) Crigler–Najjar syndrome type 1
- (D) Crigler–Najjar syndrome type 2

**The answer is B: Gilbert syndrome.** This type of question is very common on the Internal Medicine shelf examination. Distinguishing the causes of predominantly unconjugated hyperbilirubinemia is high yield for the test. In this patient, we see that her total bilirubin is slightly elevated at 3.1 mg/dL; given that the indirect bilirubin makes up the majority of this (2.9 mg/dL), we know that it is unconjugated hyperbilirubinemia. Elevated unconjugated (indirect) bilirubin levels are due to either hemolysis or a defect in bilirubin conjugation. Gilbert syndrome is a common cause of *mild* unconjugated hyperbilirubinemia and results from decreased production of the enzyme that facilitates conjugation of bilirubin with glucuronic acid, UDP glucuronosyltransferase. The enzyme still functions normally; there is just a decreased concentration of the enzyme. Gilbert syndrome is always mild in nature, with mild icterus as the only physical examination finding. Patients present with very nonspecific complaints like fatigue and usually report stress, fasting, or illness as triggers.

(A) G6PD deficiency will cause unconjugated hyperbilirubinemia (from hemolysis), but would present with anemia, which this patient does not have. (C) Crigler–Najjar syndrome type 1 is a rare cause of unconjugated hyperbilirubinemia that is characterized by complete *absence* of UDP glucuronosyltransferase, resulting in extremely elevated indirect bilirubin levels (20 to 50 mg/dL). Although phototherapy is helpful for short-term results, liver transplant is the only option to cure this disorder. Before these treatment options, children usually died from kernicterus (bilirubin encephalopathy). (D) Crigler–Najjar syndrome type 2 is less severe than type 1 and is distinguished by lower indirect bilirubin levels (<20 mg/dL). Of note, UDP glucuronosyltransferase is present but at reduced levels with this condition. Treatment with phenobarbital will reduce serum bilirubin levels.

**20** A 71-year-old woman with a history of peptic ulcer disease (PUD), diabetes, and hypertension presents with severe epigastric pain that has radiated to her back and down both arms for the last 3 hours. She also reports nausea, vomiting, and some shortness of breath. She has a temperature of 37°C, blood pressure of 98/64 mmHg, heart rate of 110 beats per minute, and a respiratory rate of 20 breaths per minute. Physical examination is significant for tenderness to deep palpation in the epigastrium without guarding or rebound. Murphy sign is negative.

Which of the following is the best next step in management?

- (A) Amylase and lipase levels
- (B) Electrocardiogram (ECG)
- (C) Abdominal x-ray
- (D) Fecal occult blood test (FOBT)

**The answer is B: Electrocardiogram (ECG).** The patient in this question is presenting with abdominal pain that radiates both to her back and down her arms. Given the radiation down her arms, a myocardial infarction (MI) must be ruled out. An MI can present with abdominal pain (particularly inferior and posterior infarctions), especially in diabetic patients with shortness of breath. When an MI is suspected, an ECG and troponin levels should be ordered immediately. (A) Although acute pancreatitis might be the diagnosis, immediate life-threatening diagnoses (such as an MI) must be excluded prior to further workup. (C) Abdominal x-ray would be the best test if perforated PUD were suspected. However, this patient does not present with rebound or peritoneal irritation on physical examination. (D) An FOBT is not warranted at this time, as she is showing no signs of a GI bleed.



A 27-year-old woman of Jewish descent presents with jaundice for the last week. She reports recently “battling a stubborn cold.” She has no other complaints and her past medical history is only significant for chronic rhinosinusitis. Laboratory studies reveal the following.

|                            |           |
|----------------------------|-----------|
| Total bilirubin            | 4.2 mg/dL |
| Indirect bilirubin         | 0.5 mg/dL |
| Direct bilirubin           | 3.7 mg/dL |
| Aspartate aminotransferase | 22 U/L    |
| Alanine aminotransferase   | 21 U/L    |
| Alkaline phosphatase       | 64 U/L    |

After a thorough chart review, it was discovered she had a liver biopsy performed 3 years prior to her visit, which revealed black granular pigment in the majority of hepatocytes.

Which of the following is the most likely diagnosis?

- (A) Gilbert syndrome
- (B) Dubin–Johnson syndrome
- (C) Rotor syndrome
- (D) Crigler–Najjar syndrome type 2

**The answer is B: Dubin–Johnson syndrome.** The patient in this question is presenting with conjugated hyperbilirubinemia with dark granular pigment present within hepatocytes. This is consistent with a diagnosis of the rare condition called Dubin–Johnson syndrome. This benign condition is most common in Jewish patients and presents clinically with jaundice and nonspecific complaints (fatigue, abdominal pain, malaise). The jaundice is very mild and usually only becomes apparent during an illness or oral contraceptive use. The problem in this condition is mildly defective bile secretion that results in conjugated hyperbilirubinemia. The liver is grossly black due to epinephrine metabolites located within the lysosomes (giving a dark granular appearance of the hepatocytes). Prognosis is excellent so treatment is not warranted (other than minimizing triggers). (A) Gilbert syndrome is characterized by *unconjugated* hyperbilirubinemia. (C) Rotor syndrome is also a disorder of hepatic bile secretion; however, hyperbilirubinemia of both unconjugated and conjugated bilirubin is seen and there are no pigmented granules in the hepatocytes. (D) Crigler–Najjar syndrome type 2 is characterized by *unconjugated* hyperbilirubinemia.

22

A 37-year-old man with a history of ulcerative colitis controlled with 5-aminosalicylic acid presents with malaise, pruritus, and fatigue for the past 4 months. He reports no fever, chills, or weight loss and takes no other medications. He has a temperature of 37°C, blood pressure of 118/80 mmHg, heart rate of 82 beats per minute, and a respiratory rate of 20 breaths per minute. Physical examination reveals tenderness to palpation in the right upper quadrant. There is no hepatomegaly and Murphy sign is negative. Laboratory results reveal an alkaline phosphatase level of 910 U/L, erythrocyte sedimentation rate (ESR) of 160 mm/h, and a positive p-ANCA antibody.

Which of the following is the most likely diagnosis in this patient?

- (A) Microscopic polyangiitis
- (B) Primary biliary cirrhosis
- (C) Drug toxicity
- (D) Primary sclerosing cholangitis

**The answer is D: Primary sclerosing cholangitis.** This patient is presenting with signs, symptoms, and laboratory findings consistent with a diagnosis of primary sclerosing cholangitis (PSC), a chronic inflammatory disorder associated with fibrosis and stricturing of medium-sized and large intra- and extrahepatic bile ducts. Ultimately the bile duct destruction will cause end-stage liver disease. Of note, the vast majority of patients who present with PSC have a diagnosis of ulcerative colitis. Patients typically present with pruritus and fatigue and laboratory tests reveal severely elevated alkaline phosphatase and bilirubin. Other associated findings include the presence of p-ANCA antibodies and elevated inflammatory markers. ERCP will demonstrate “beading”

and liver biopsy typically shows periductal “onion-skin” fibrosis in addition to intrahepatic ductal destruction with lymphocytic infiltration. **(A)** Microscopic polyangiitis is a poorly understood autoimmune small-vessel vasculitis that is associated with p-ANCA antibodies. **(B)** Primary biliary cirrhosis is more common in women and is associated with anti-mitochondrial antibodies. **(C)** Drug toxicity often presents with acute hepatitis with severely elevated AST and ALT levels; however, this patient is only taking 5-ASA for his ulcerative colitis.

23

A 37-year-old man presents with weakness, fatigue, polydipsia, polyuria, and increased “skin color” for the last 4 months. Physical examination reveals hepatomegaly. Laboratory results reveal the following.

|                            |                                      |
|----------------------------|--------------------------------------|
| Aspartate aminotransferase | 138 U/L                              |
| Alanine aminotransferase   | 136 U/L                              |
| Blood glucose              | 210 mg/dL                            |
| Transferrin saturation     | 62%                                  |
| Serum ferritin             | 1,610 ng/mL (normal 12 to 300 ng/mL) |

Which of the following malignancies is this patient at risk for?

- (A)** Cholangiocarcinoma
- (B)** Renal cell carcinoma
- (C)** Pancreatic cancer
- (D)** Hepatocellular carcinoma

**The answer is D: Hepatocellular carcinoma.** This patient is presenting with signs and symptoms consistent with a diagnosis of hereditary hemochromatosis, an autosomal recessive disorder that leads to increased iron deposition in various organs. “Bronze diabetes” is a term coined for this condition since patients often develop new-onset diabetes and skin hyperpigmentation. Iron deposition in the liver causes hepatomegaly (as seen in this patient), an elevated AST and ALT, and eventually cirrhosis. Diagnosis is suggested by elevated transferrin saturation (>45%) and serum ferritin levels (>200 ng/mL). If untreated, patients are at a significantly increased risk for developing hepatocellular carcinoma. **(A)** Cholangiocarcinoma originates in the bile ducts and is not associated with hereditary hemochromatosis. **(B)** Renal cell carcinoma has no relationship with hereditary hemochromatosis. **(C)** Pancreatic cancer may result from chronic pancreatitis, not hereditary hemochromatosis.

24

A 34-year-old man presents to the physician with right upper quadrant pain that began shortly after eating dinner at a Chinese restaurant. He describes the pain as “stabbing” and radiating to his right scapular region. He has vomited two times. He has an unremarkable past medical history but reportedly drinks 8 to 10 beers per day. Family history is significant for breast cancer on his mother’s side and rheumatoid arthritis on his father’s side. He has a temperature of 38.6°C, blood pressure of 118/80 mmHg, heart rate of 82 beats per minute, and a respiratory rate of 20 breaths per minute. Physical examination shows severe right upper quadrant pain on deep palpation, most pronounced on palpation after deep inspiration. Laboratory results reveal the following.

|                            |                        |
|----------------------------|------------------------|
| Aspartate aminotransferase | 51 U/L                 |
| Alanine aminotransferase   | 48 U/L                 |
| Alkaline phosphatase       | 70 U/L                 |
| Total bilirubin            | 1.4 mg/dL              |
| Direct bilirubin           | 0.7 mg/dL              |
| Amylase                    | 96 U/L                 |
| Leukocyte count            | 18,000/mm <sup>3</sup> |

Which of the following is contributing to this patient’s disorder?

- (A) Alcoholic liver disease
- (B) Gallstone obstruction in the cystic duct
- (C) Obstruction from carcinoma of the head of the pancreas
- (D) Gallstone obstruction in the common bile duct

**The answer is B: Gallstone obstruction in the cystic duct.** The patient in this question is presenting with acute cholecystitis. He is presenting with fever, right upper quadrant pain after a fatty meal that radiates to the right scapula, and positive Murphy sign (pain on palpation in the right upper quadrant with cessation of inspiration). Additional nonspecific findings include vomiting, leukocytosis, and mild elevation in transaminases. Acute cholecystitis usually arises from gallstone formation that obstructs the cystic duct. The symptoms occur after eating a fatty meal because the fat stimulates gallbladder contraction and, in the presence of cystic duct obstruction, this leads to colicky pain. Infection results from stasis that contributes to bacterial growth in the gallbladder. (D) Importantly, alkaline phosphatase is *not* elevated in this

patient with acute cholecystitis. If it were elevated (in addition to total bilirubin and direct bilirubin), this might indicate common bile duct obstruction in the setting of jaundice (choledocholithiasis). (A) Alcoholic liver disease does not present with this constellation of symptoms. (C) Similar to common bile duct obstruction, obstruction from a carcinoma of the head of the pancreas would cause severely elevated alkaline phosphatase levels and would normally present with weight loss and painless jaundice.

25

A 52-year-old woman presents with confusion that has worsened over the past week. Her partner reports that she has also noticed yellowing of the skin. Further history reveals that the patient has been taking a significant amount of over-the-counter pain medications due to diffuse joint pain. The patient drinks three glasses of wine per night and reports no illicit drug use. Physical examination is significant for tenderness to palpation in the right upper quadrant and hepatomegaly. Laboratory results reveal the following.

|                             |           |
|-----------------------------|-----------|
| Total bilirubin             | 7.1 mg/dL |
| Direct bilirubin            | 4.2 mg/dL |
| Aspartate aminotransferase  | 5,424 U/L |
| Alanine aminotransferase    | 6,934 U/L |
| Alkaline phosphatase        | 120 U/L   |
| Prothrombin time            | 31 s      |
| Partial thromboplastin time | 44 s      |
| INR                         | 1.9       |

Which of the following is the underlying diagnosis?

- (A) Drug-induced acute liver failure
- (B) Acute alcoholic hepatitis
- (C) Nonalcoholic fatty liver disease
- (D) Chronic viral hepatitis

**The answer is A: Drug-induced acute liver failure.** This patient is presenting with signs and symptoms consistent with a diagnosis of acute liver failure. Acute liver failure is distinguished by severely elevated transaminases, defective hepatic synthesis (coagulation abnormalities, elevated bilirubin), and hepatic encephalopathy. The most common causes of acute liver failure include

medications, viral hepatitis, ischemic hepatopathy, acute fatty liver of pregnancy, and HELLP syndrome. Given this patient's history of over-the-counter pain medications (likely acetaminophen), the diagnosis is likely drug-induced acute liver failure. Acetaminophen levels should be determined and the patient should begin treatment with *N*-acetylcysteine. **(B)** Acute alcoholic hepatitis alone usually only causes a mild to moderate elevation of AST and ALT levels. In addition, the AST:ALT ratio is usually greater than 2:1. **(C)** Nonalcoholic fatty liver disease is usually asymptomatic and presents with only mild elevations of AST and ALT levels. It is usually chronic in nature and mental status changes are rare, though in rare cases it can progress to end stage liver disease (ESLD). **(D)** Similar to nonalcoholic liver disease, chronic viral hepatitis is associated with mild elevations of AST and ALT levels and will not present with abnormal coagulation studies or hepatic encephalopathy. It also would not present with a 1- to 2-week course.

26

A 62-year-old woman presents with nausea, vomiting, and epigastric pain. She has a history of chronic pancreatitis and consumes three to four glasses of wine per day. She endorses a 9.1-kg (20-lb) weight loss over the last 4 months and reports increased flatulence and “floating stools.” Physical examination reveals nonspecific abdominal pain to deep palpation in the epigastric region in addition to the finding seen in the photo below (*Figure 4-4*).



**Figure 4-4**



Which of the following is the most appropriate imaging modality for this patient?

- (A) Abdominal upright x-ray
- (B) ERCP
- (C) Abdominal CT scan
- (D) Abdominal MRI

**The answer is C: Abdominal CT scan.** The patient in this question is presenting with signs and symptoms suspicious for pancreatic cancer. The patient's history of chronic pancreatitis, scleral icterus, and weight loss is consistent with pancreatic cancer. Several of the patient's symptoms can be explained by chronic pancreatitis, but the jaundice that is present makes pancreatic cancer the likely diagnosis. CT scan of the abdomen is the best imaging modality for patients with suspected pancreatic cancer. (A) Abdominal upright x-rays are helpful in chronic pancreatitis for detecting calcifications. They are not useful in diagnosing pancreatic cancer. (B) ERCP is useful in cases where CT scan is unable to reveal a tumor within the pancreas. However, this is not the initial imaging modality of choice. (D) Abdominal MRI is a good option for patients with pancreatic duct obstruction who are unable to undergo ERCP. However, CT scan is still the best, and most sensitive, imaging modality for detecting pancreatic cancer.

27

A 67-year-old woman presents for routine medical screening. Her only complaints are mild constipation and periodic headaches, but she reports that she has had these symptoms for several years. She denies fevers, chills, night sweats, or weight loss. She drinks one glass of wine per day. Physical examination including vital signs is unremarkable and complete blood count (CBC) is within normal limits. Fecal occult blood test (FOBT) is negative. As part of routine medical screening, she receives a colonoscopy that reveals several diverticula in the sigmoid colon. The patient is concerned and would like to know how to best manage this condition.

Which of the following recommendations should be offered to this patient?

- (A) Prophylactic antibiotics to prevent the development of diverticulitis
- (B) Increase in dietary fiber
- (C) Complete alcohol abstinence
- (D) Elective surgery to prevent the development of diverticulitis

**The answer is B: Increase in dietary fiber.** This patient is presenting with uncomplicated diverticulosis. As people age, diverticula (sac-like protrusions at weak areas in the wall of the colon) are more likely to form.

Uncomplicated, asymptomatic diverticulosis is most common, but diverticulosis can also present with abdominal pain and worsening constipation. Due to the elevated colonic pressure generated in constipation, diverticula can protrude more readily through weak areas in the colonic wall. The most effective management of uncomplicated diverticulosis is dietary modifications, specifically increasing the daily intake of fiber in one's diet. This creates the formation of bulky stools that minimize the occurrence of diverticula. Laxatives are also helpful in reducing constipation, thereby minimizing the colonic pressure that favors the formation of diverticula. (A) Antibiotics are important in the treatment of diverticulitis; however, diverticulitis is accompanied by fever, leukocytosis, and abdominal pain on physical examination. (C) Refraining from alcohol consumption is beneficial on many levels, but has not been shown to have an effect on diverticular disease. (D) Elective surgery is too extreme of an option given the patient's lack of symptoms. Surgical intervention is recommended in the setting of complications (bleeding, perforation, etc.).

28

A 62-year-old woman with a history of hepatitis C infection presents with confusion that has worsened over the past week. Further history reveals that the patient has been vomiting bright red blood recently. The patient was an IV drug user several years previously but endorses no current drug or alcohol use. Physical examination is significant for a confused and disoriented female. Abdominal examination reveals shifting dullness in addition to the finding below (*Figure 4-5*). When the patient extends her arms out in front of her, a jerking movement of the limbs is observed.



**Figure 4-5**

Laboratory results reveal the following.

|                     |                         |
|---------------------|-------------------------|
| Sodium              | 132 mEq/L               |
| Potassium           | 3.3 mEq/L               |
| Chloride            | 95 mEq/L                |
| Bicarbonate         | 22 mEq/L                |
| Blood urea nitrogen | 38 mg/dL                |
| Creatinine          | 0.7 mg/dL               |
| Hematocrit          | 29%                     |
| Leukocyte count     | 3,000/mm <sup>3</sup>   |
| Platelets           | 120,000/mm <sup>3</sup> |

Which of the following is the most appropriate treatment at this time?

- (A) Furosemide
- (B) Thiamine
- (C) Lactulose
- (D) Morphine

**The answer is C: Lactulose.** This patient is presenting with signs and symptoms of cirrhosis (ascites, spider angiomas) and hepatic encephalopathy (altered mental status and asterix). In hepatic encephalopathy, the liver is unable to convert ammonia into urea and it therefore accumulates, in addition to other toxins the liver is unable to clear. It is often precipitated by illness or gastrointestinal bleed (as in this patient with hematemesis). Increased ammonia levels can assist in making the diagnosis, but the diagnosis is ultimately clinical and can cause confusion in the correct setting of end-stage liver disease (ESLD). Treatment involves treating the precipitant and decreasing serum ammonia levels (however, even if one uses ammonia to help with diagnosis, it is not necessary to follow ammonia levels; rather, one should follow clinical improvement). Lactulose, a nonabsorbable disaccharide, is used because bacteria in the gut metabolize it into acidic compounds (lactic acid, acetic acid) that permit the *absorbable* ammonia to be converted into the *nonabsorbable* ammonium, thereby enabling excretion from the body. (A) Furosemide would improve the ascites and volume status in a cirrhotic patient, but is not helpful in the management of hepatic encephalopathy. (B) Thiamine is useful in the treatment of *Wernicke encephalopathy*, another form of encephalopathy characterized by altered mental status, ataxia, and nystagmus and is associated with thiamine deficiency. Of note, asterix is not present in Wernicke encephalopathy. (D) Morphine is a narcotic that would be challenging for a cirrhotic patient to metabolize.

**29** A 62-year-old man presents with 3 days of abdominal pain and vomiting. He has not had a bowel movement in 4 days and has not passed gas for the past 3 days. He has a temperature of 38.6°C, blood pressure of 118/80 mmHg, heart rate of 110 beats per minute, and a respiratory rate of 22 breaths per minute. Physical examination reveals a distended abdomen that is diffusely tender to palpation without guarding or rebound. Bowel sounds are difficult to appreciate. Laboratory results reveal the following.

|                 |                        |
|-----------------|------------------------|
| Hemoglobin      | 13.6 g/dL              |
| Leukocyte count | 13,500/mm <sup>3</sup> |
| Amylase         | 132 U/L                |

What is the best next step in the diagnostic workup for this patient?

- (A) Abdominal ultrasound
- (B) Colonoscopy
- (C) Abdominal x-ray
- (D) Sigmoidoscopy

**The answer is C: Abdominal x-ray.** The patient in this question is presenting with signs and symptoms concerning for a small-bowel obstruction (SBO). The typical constellation of symptoms includes abdominal pain, vomiting, obstipation, abdominal distention, and diffuse tenderness. A mild leukocytosis and elevated amylase is often found in an SBO. The best initial test is an abdominal x-ray because it often reveals dilated bowel loops and several air-fluid levels. Treatment involves supportive care, bowel rest, and decompression with a nasogastric tube. Surgery is reserved for those patients who fail to improve with the aforementioned treatments and/or develop findings consistent with strangulation. (A, B, D) These options are not the best *initial* test in diagnosing an SBO.

**30** A 34-year-old woman with a history of bipolar disorder presents with abdominal pain and diarrhea for the past week. She reports nonbloody watery stools at a frequency of 20 to 25 times per day. She is unable to sleep due to the diarrhea and is hopeful that she can receive treatment for her disorder. She has had several visits in the past 5 years for similar complaints. A physical examination including vital signs is unremarkable. A thorough chart review was performed and it was found that she had a lower GI endoscopy at a previous visit that demonstrated brownish black discoloration of the colonic wall with pale lymph follicles.

Which is the most likely diagnosis in this patient?

- (A) Irritable bowel syndrome (IBS)
- (B) Celiac disease
- (C) Ulcerative colitis
- (D) Laxative abuse

**The answer is D: Laxative abuse.** The patient in this question is presenting with signs and symptoms consistent with factitious diarrhea secondary to laxative abuse. The description, frequency, and nocturnal presence of her diarrhea are suggestive of the diagnosis. Furthermore, she has had multiple visits in the past for similar symptoms. The diagnosis is ultimately confirmed with biopsy that shows dark brown discoloration of the colon with pale lymph follicles. (A) IBS is not associated with *nocturnal* diarrhea. (B, C) Celiac disease and ulcerative colitis do not present with colonic brown discoloration with interspersed pale lymph follicles.

31

A 27-year-old medical student who recently (3 weeks ago) began a 9-month treatment of isoniazid for latent tuberculosis after a positive purified protein derivative (PPD) test presents for follow-up. He has no complaints and reports refraining entirely from alcohol use. Physical examination is unremarkable and laboratory results reveal the following:

|                            |           |
|----------------------------|-----------|
| Total bilirubin            | 0.7 mg/dL |
| Direct bilirubin           | 0.3 mg/dL |
| Aspartate aminotransferase | 72 U/L    |
| Alanine aminotransferase   | 93 U/L    |
| Alkaline phosphatase       | 51 U/L    |

Which of the following is the next best step in management of this patient?

- (A) Continue current treatment regimen
- (B) Replace isoniazid with alternative anti-tuberculosis medication
- (C) Liver biopsy
- (D) Discontinue all anti-tuberculosis medications

**The answer is A: Continue current treatment regimen.** A 9-month course of isoniazid (INH) is recommended for latent tuberculosis infection. INH is also used in active tuberculosis infection with rifampin, ethambutol, and pyrazinamide. A mild hepatotoxicity can occur in some patient on INH

therapy. The risk of hepatotoxicity on INH treatment increases if the patient consumes alcohol during the treatment regimen. Nevertheless, up to 20% of patients on INH will encounter a mild hepatic injury regardless of alcohol use with mild increases in ALT and AST (usually <100 U/L). This is self-limited though and does not affect the prognosis of the patient. The recommendation is to continue the INH treatment with close follow-up and monitoring of liver function tests.

(B) A second-line anti-tuberculosis medication can be used in cases of severe hepatotoxicity (which this patient does not demonstrate). (C) A liver biopsy is important in cases of unknown etiology. The AST/ALT elevations here are known to be due to INH treatment, making it unnecessary to perform a liver biopsy. (D) Three weeks is not sufficient time to clear the latent *Mycobacterium tuberculosis* infection, so all anti-tuberculosis medications should not be discontinued.



A 64-year-old man is on his third postoperative day after a partial small bowel resection and is noted to have jaundice. The surgery was successful and the patient had no complications intraoperatively other than a few mild hypotensive episodes for which he received three units of packed red blood cells. The patient is afebrile and the physical examination demonstrates jaundice. Abdominal examination demonstrates a soft nontender, nondistended abdomen. Laboratory results reveal the following.

|                                   |           |
|-----------------------------------|-----------|
| Total bilirubin                   | 7.7 mg/dL |
| Direct bilirubin                  | 5.3 mg/dL |
| Aspartate aminotransferase        | 61 U/L    |
| Alanine aminotransferase          | 58 U/L    |
| Alkaline phosphatase              | 310 U/L   |
| Amylase                           | 52 U/L    |
| Prothrombin time (PT)             | 14 s      |
| Partial thromboplastin time (PTT) | 36 s      |

Which of the following is the most likely diagnosis?

- (A) Postoperative cholestasis
- (B) Drug-induced acute liver failure
- (C) Posttransfusion hepatitis
- (D) Normal postoperative finding

**The answer is A: Postoperative cholestasis.** The patient in this question is showing signs, symptoms, and laboratory findings consistent with a diagnosis of postoperative cholestasis. This condition is benign and commonly occurs after surgeries with hypotension and significant blood loss. The jaundice that develops with this condition is thought to occur from decreased liver function (thought to be secondary to the hypotensive episodes) and diminished bilirubin clearance (thought to be secondary to renal tubular necrosis). Jaundice occurs by the third postoperative day and laboratory findings typically show elevated total bilirubin and alkaline phosphatase levels. **(B)** Acute liver failure is associated with coagulation abnormalities (not seen in this patient) and hepatic encephalopathy. **(C)** Unlike in the past, posttransfusion hepatitis is exceedingly rare nowadays since blood products are thoroughly screened. **(D)** Although this condition is benign, this is not to (and should not) be considered a normal postoperative finding. Bilirubin levels should be monitored to demonstrate improvement of the cholestasis.



A 31-year-old woman presents with anxiety that she might have contracted viral hepatitis. She is a volunteer at the local hospital and although she reports no needle stick injuries or direct exposure to blood, she is concerned because 5 months ago she was observing a paracentesis without eye protection on a patient with chronic hepatitis B infection and she reports that ascites fluid splashed into her eyes as the physician was completing the procedure. Hepatitis B panel is ordered and reveals the following.

|            |          |
|------------|----------|
| HBsAg      | Negative |
| Anti-HBsAg | Positive |
| Anti-HBcAg | Negative |
| HBeAg      | Negative |
| Anti-HBeAg | Negative |

What is the patient's status with respect to hepatitis B infection?

- (A)** Chronic hepatitis B infection
- (B)** Vaccination against hepatitis B infection
- (C)** Previous hepatitis B infection, but fully recovered
- (D)** Acute hepatitis B infection

**The answer is B: Vaccination against hepatitis B infection.** The patient in this question would like to know whether or not she contracted hepatitis B (HBV) infection from her ascites exposure. In this case, the patient presents

with positive anti-HBsAg but negative HBsAg and other HBV serologic tests. This is consistent with vaccination against hepatitis B. Anti-HBsAg appears in the serum after HBV vaccination or elimination of HBsAg, so this is detectable for life and signifies a noninfective state and immunity. Of note, there is a period called the “window period” in which there is a period of time between the elimination of HBsAg and appearance of anti-HBsAg. See *Figure 4-6* for full details. **(A)** Chronic HBV infection would have positive HBsAg (must be present for more than 6 months to be chronic). **(C)** Previous hepatitis B infection with full recovery would be positive for anti-HBsAg (as in this patient) and negative for HBsAg. However, these patients will also be positive for anti-HBcAg against the viral core antigen HBcAg. This will not be found in vaccinated individuals, as the HBV vaccine does not contain core antigen. **(D)** Acute hepatitis B infection would have positive HBcAb, specifically IgM. This is in contrast to a chronic carrier state in which there is positive HBcAb, but it is IgG. Other serologic markers characteristic of acute hepatitis B infection include positive HBsAg and negative HBsAb (too early to mount a response yet).

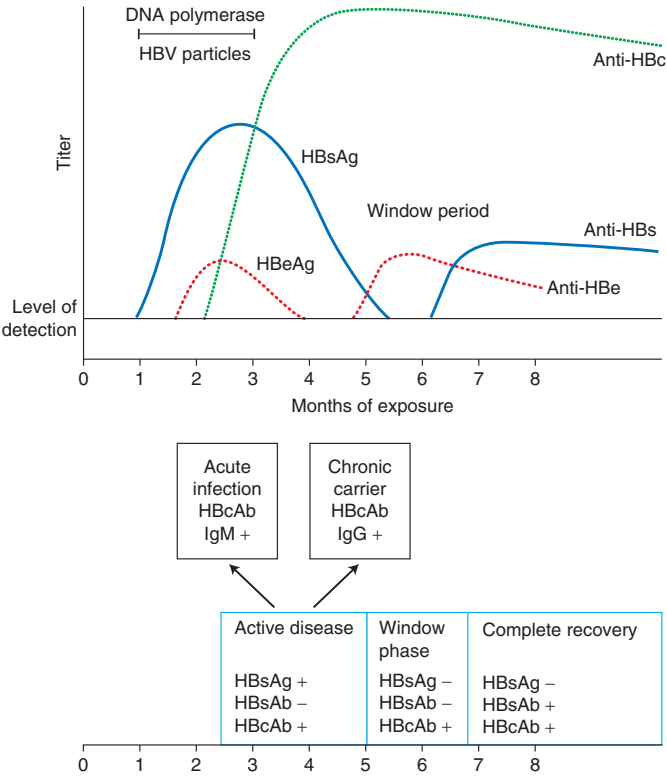


Figure 4-6



34

A 71-year-old man with a history of hypertension presents with cough, foul breath, a sense of having a “lump” in his neck, and subjective fevers. He reports that he has had much difficulty swallowing his meals and admits to often regurgitating undigested food particles. He has a temperature of 38.5°C, blood pressure of 132/90 mmHg, heart rate of 104 beats per minute, and a respiratory rate of 18 breaths per minute. Physical examination is significant for foul-smelling breath, but is otherwise unremarkable.

Which of the following is the best next step in the diagnostic workup of this patient?

- (A) Upper GI endoscopy
- (B) Esophagram barium swallow study
- (C) Bronchoscopy
- (D) Placement of gastric tube for feeding

**The answer is B: Esophagram barium swallow study.** The patient is presenting with signs and symptoms (halitosis, cough, dysphagia, sense of throat “lump”) consistent with a presumptive diagnosis of Zenker diverticulum, a diverticulum of the mucosa of the pharynx just above the upper sphincter of the esophagus. It is a false diverticulum (not involving all layers of the esophageal wall). The halitosis results from settling of the food material in the diverticulum. Occasionally, one can palpate a Zenker diverticulum (if large) and patients are at risk for aspiration pneumonia. The best diagnostic test to order is an esophagram barium swallow study. Definitive treatment is surgical intervention. (A) Upper GI endoscopy is contraindicated when Zenker diverticulum is suspected, as it can potentially cause perforation. (C) Bronchoscopy might be indicated if this patient had presented with recurrent pneumonias consistent with an obstructing mass, but that is not the case in this scenario. (D) Gastric feeding tube placement is not indicated as Zenker diverticulum is treated with surgery and the patient will be able to resume his normal dietary habits.

35

A 39-year-old man with a history of alcoholism presents with 2 days of unrelenting midepigastic abdominal pain that radiates to the back. The patient reports some relief with leaning forward. He has vomited several times and is febrile. The patient reports drinking 10 to 12 beers per day for the last 15 years. Laboratory findings reveal severely elevated amylase and lipase and chest x-ray confirms left pleural effusion and an elevated hemidiaphragm.

Which of the following is the best initial treatment for this patient's condition?

- (A) Broad-spectrum antibiotics
- (B) Corticosteroids
- (C) Supportive care
- (D) Administration of pancreatic enzymes and vitamin B<sub>12</sub>

**The answer is C: Supportive care.** The patient in this question is presenting with classic symptoms and laboratory values consistent with a diagnosis of acute pancreatitis (midpigastic abdominal pain that radiates to the back, vomiting, elevated lipase and amylase, pleural effusion). The best treatment initially with acute pancreatitis is supportive management consisting of making the patient nil per os (NPO), administration of IV fluids, and pain management. **(A)** Broad-spectrum antibiotics are often used in the treatment of *severe* pancreatitis (often associated with signs of hemorrhage, i.e., Grey Turner sign of flank ecchymoses). The antibiotic of choice is typically imipenem. **(B)** Corticosteroids are not useful in the treatment of acute pancreatitis. **(D)** Administration of pancreatic enzymes and vitamin B<sub>12</sub> is used in the treatment of *chronic* pancreatitis, not acute pancreatitis.

**36** A 58-year-old male is being treated for *Pseudomonas* nosocomial pneumonia with cefepime. His symptoms improve, but 1 week later he develops fever and diarrhea with several loose nonbloody stools per day.

Given the likely diagnosis in this scenario, what is the treatment of choice?

- (A)** Ciprofloxacin
- (B)** Clindamycin
- (C)** Imipenem
- (D)** Metronidazole

**The answer is D: Metronidazole.** The patient in this clinical scenario has likely developed *Clostridium difficile*-associated diarrhea (CDAD). This gram-positive spore-forming bacterium is best known for causing antibiotic-associated diarrhea. It typically develops after treatment with fluoroquinolones, cephalosporins (as with this patient), carbapenems, or clindamycin. It can cause pseudomembranous colitis and rarely progresses to toxic megacolon. The treatment of choice is metronidazole with oral vancomycin being reserved for severe or in some cases of recurrent CDAD. Oral vancomycin is used instead of IV vancomycin because oral vancomycin is not absorbed from the gut into the bloodstream and therefore has maximum efficacy. **(A, B, C)** These antibiotics are associated with the development of CDAD and should not be used as treatment.

**37** A 67-year-old woman of Japanese descent presents with 5 months of vomiting undigested food, hematemesis, and a 6.8-kg (15-lb) weight loss. Physical examination reveals a woman with tachycardia, conjunctival pallor, and a nontender, slightly mobile mass in the midpigastic region. The patient is noted to have hyperpigmented velvety plaques in her bilateral axillary regions and the base of her neck.

Which of the following is the most appropriate next step in management?

- (A) Abdominal ultrasound
- (B) Upper GI endoscopy
- (C) Barium swallow study
- (D) *H. pylori* serologic testing

**The answer is B: Upper GI endoscopy.** The patient in this question is presenting with signs and symptoms concerning for gastric cancer. Symptoms of gastric cancer are very nonspecific and include weight loss, loss of appetite, abdominal discomfort, weakness, fatigue, nausea, vomiting, hematemesis, and many others. Risk factors for gastric cancer include *H. pylori* infection, smoking, and dietary intake of smoked foods or nitrates/nitrites in cured meats. Upper GI endoscopy is the diagnostic method of choice as the tumor can be visualized and abnormal tissue biopsied. Gastric cancer is also associated with acanthosis nigricans (as seen on dermatologic examination with this patient). (A, C) Abdominal ultrasound and barium swallow study will not permit biopsy of tissue, so they are not the preferred diagnostic modality. (D) *H. pylori* serologic testing might be performed to evaluate for risk factors, but will not determine the underlying diagnosis of gastric cancer. Tissue must be biopsied to establish the diagnosis.

38

A 27-year-old woman presents with anorexia, nausea, vomiting, and fever for the past 3 weeks. She reports that several of her friends have told her she looks “yellow.” Physical examination is significant for an enlarged and tender liver and jaundice. Viral hepatitis panel is ordered and demonstrates positive HCV RNA and anti-HCV antibody, consistent with hepatitis C infection.

Which of the following findings is NOT a risk factor for hepatitis C infection?

- (A) Blood transfusion
- (B) Contaminated food
- (C) Intravenous drug use
- (D) Sexual contact

**The answer is B: Contaminated food.** The patient in this question has acute hepatitis C (HCV) infection. HCV is largely transmitted through IV drug use and blood transfusions (although blood transfusion transmission is exceedingly rare nowadays due to thorough blood screening). Much less commonly, HCV can be transmitted through sexual contact (but this is *very* uncommon for HCV and much more common in HBV transmission). Contaminated food and water is the cause of hepatitis A (HAV) infection through fecal–oral transmission and is not associated with HCV infection. Of all the viral hepatitis, hepatitis C infection is the most likely to become chronic (70% to 80% of HCV infections become chronic).

39

A 29-year-old woman presents with abdominal pain for the last 7 days. She describes the pain as “dull” and localized to the right upper quadrant. It does not radiate. She has a history of asthma and has taken oral contraceptive medication for birth control for the last 8 years. She reports no more than two to three glasses of wine per week and she does not use illicit drugs. She denies weight loss, fatigue, fevers, or chills. On physical examination, a palpable mass is appreciated in the right upper quadrant. Laboratory results are significant for an elevated gamma glutamyl transpeptidase (103 U/L) and elevated alkaline phosphatase (224 U/L). All other liver function tests are within normal limits.

Which is the most likely diagnosis in this patient?

- (A) Hepatocellular carcinoma
- (B) Hepatic adenoma
- (C) Echinococcal (hydatid) cyst
- (D) Alcoholic hepatitis

**The answer is B: Hepatic adenoma.** The patient in this question is presenting with a history and symptoms consistent with hepatic adenoma (also known as hepatocellular adenoma). This is a relatively rare benign liver tumor that is associated with hormonal contraceptive medications with a high estrogen level. The mechanism of action for this association is not entirely known. A hepatic adenoma is usually diagnosed when patients (typically middle-aged women) present with abdominal pain in the right upper quadrant or when a patient collapses from rupture of the hepatic adenoma. Given the susceptibility to rupture, biopsy of the hepatic adenoma is contraindicated. In addition to a palpable right upper quadrant mass, findings occasionally include jaundice. Although liver function tests are typically normal, the most common abnormal laboratory tests include elevated gamma glutamyl transpeptidase and alkaline phosphatase. Of note, close to 10% of hepatic adenomas can turn malignant which is why  $\alpha$ -fetoprotein levels are important to monitor in these patients. Surgical removal is only indicated with symptomatic hepatic adenomas. With asymptomatic hepatic adenomas, the recommendation is to discontinue oral contraceptive medications and monitor with serial  $\alpha$ -fetoprotein levels (to ensure malignant transformation has not occurred).

(A) Hepatocellular carcinoma is highly unlikely given this patient's young age, lack of heavy alcohol use, and no history of viral hepatitis. (C) Echinococcal (hydatid) cysts can present with similar vague abdominal complaints; however, this is a parasitic infection by a tapeworm. It is not endemic in the United States, so on the Internal Medicine shelf examination a history of recent immigration is likely to be present. (D) Alcoholic hepatitis would be highly improbable given the patient's alcohol history (two to three glasses of wine per week).

40

A 51-year-old man with a history of chronic hepatitis C infection presents for follow-up. His only complaints include fatigue and “red dots” on his torso. Physical examination reveals spider angiomas as well as

splenomegaly and evidence of mild ascites. Abdominal ultrasound at a previous visit showed a shrunken liver consistent with cirrhosis.

Which of the following screening tools is needed in the management of this patient?

- (A) Ammonia levels
- (B) Liver biopsy
- (C) Upper GI endoscopy
- (D) Close observation and routine follow-up

**The answer is C: Upper GI endoscopy.** The patient in this question is presenting with *compensated* cirrhosis due to chronic viral hepatitis C infection. The first step in determining appropriate management for cirrhotic patients is to determine whether or not their condition is *compensated* (asymptomatic or nonspecific symptoms such as fatigue) or *decompensated* (upper GI bleeding, abdominal distention due to severe ascites, or mental status changes consistent with hepatic encephalopathy). In compensated cirrhosis, the goal is to prevent complications. Given the mortality associated with esophageal varices secondary to cirrhosis, it is critical that all cirrhotic patients get an upper GI endoscopy to determine the risk of variceal bleeding. Other screening modalities in *compensated* cirrhosis include ultrasound surveillance for hepatocellular carcinoma. (A) Ammonia levels are warranted if hepatic encephalopathy is suspected. However, this patient demonstrates no signs of confusion or asterixis. (B) Liver biopsy is really the only way to diagnose cirrhosis with 100% certainty, but the patient's previous ultrasound in combination with physical examination findings are highly suggestive of cirrhosis, thereby making biopsy unnecessary. (D) Close observation and routine follow-up should be done in all patients with cirrhosis. However, screening modalities are indicated to prevent decompensated cirrhosis.

41

A 26-year-old man presents with new-onset confusion, tremor, and “clumsiness” for the last 3 to 4 weeks. He decided to come in after he could not remember the name of his long-term girlfriend. He has no significant past medical history and denies alcohol or illicit drug use. Physical examination shows stable vital signs and hepatomegaly. Laboratory studies reveal the following.

|                            |           |
|----------------------------|-----------|
| Total bilirubin            | 2.0 mg/dL |
| Direct bilirubin           | 1.2 mg/dL |
| Aspartate aminotransferase | 281 U/L   |
| Alanine aminotransferase   | 269 U/L   |
| Alkaline phosphatase       | 110 U/L   |

Which of the following is the next best step in the diagnostic workup for this patient?

- (A) Liver biopsy
- (B)  $\alpha$ -1 antitrypsin levels
- (C) Lumbar puncture for cerebrospinal fluid (CSF) analysis
- (D) Serum ceruloplasmin levels

**The answer is D: Serum ceruloplasmin levels.** The patient in this question is presenting with neuropsychiatric symptoms and hepatomegaly consistent with a likely diagnosis of Wilson disease. Wilson disease is an autosomal recessive disorder in which copper accumulates in tissues due to mutations in the Wilson disease protein (ATP7B) gene; this causes a defect in incorporation of copper in hepatic lysosomes. Clinical symptoms range from an asymptomatic state to tremor, depression, and memory impairment. The diagnosis is confirmed by low serum ceruloplasmin levels (normally  $<20$  mg/dL), increased urinary copper, and Kayser–Fleischer rings (so a slit lamp examination of the eye should also be performed). (A) Liver biopsy in Wilson disease often shows inflammation, portal fibrosis, and necrotic hepatocytes. Macrovesicular steatosis and Mallory bodies may also be present. A less invasive test (such as a blood test) should be ordered before a liver biopsy is performed. (B)  $\alpha$ -1 antitrypsin levels would be ordered if  $\alpha$ -1 antitrypsin deficiency were suspected, but this disease is associated with liver and lung (emphysema in young patients) disease. (C) Lumbar puncture (LP) for CSF analysis is not useful in Wilson disease. Even though the neurologic symptoms in Wilson disease are caused from copper accumulation in the basal ganglia, this would not generate positive CSF findings.

42

A 24-year-old woman presents with a history of diarrhea. She reports returning 2 months ago from a church-affiliated hiking trip. Since returning, she has developed diarrhea, abdominal pain, and increased flatulence. Of note, she just finished taking one of her friend's ciprofloxacin for 7 days without any improvement.

Which of the following antibiotics should be prescribed to this patient?

- (A) Ampicillin
- (B) Metronidazole
- (C) Cefazolin
- (D) Extend the course of ciprofloxacin

**The answer is B: Metronidazole.** The patient in this question is presenting with classic giardiasis caused by *Giardia lamblia*. The Internal Medicine shelf examination might ask a similar question that offer clues to the diagnosis of giardiasis (history of recent travel, exposure to river water, or day care centers). This organism is common in unsanitary conditions and most often transmitted

via water (although it can also be transmitted via food). In this condition, the organism (trophozoites) sticks to the mucosa of the gut and causes malabsorption. This causes diarrhea (patients typically note foul-smelling watery stools), flatulence, abdominal pain, and sometimes weight loss. Diagnosis can be confirmed with stool studies looking for ova and parasites. Treatment is with oral metronidazole. (A, C, D) These antibiotics are not used in the treatment of giardiasis. Although ciprofloxacin is usually the best antibiotic in *infectious* diarrhea, it is not helpful in giardiasis.

43

A 51-year-old woman with a history of diabetes mellitus type 2 presents for her annual physical examination. The patient denies alcohol or drug use. Physical examination reveals an obese woman with hepatomegaly. Laboratory studies reveal the following.

|                            |           |
|----------------------------|-----------|
| Total bilirubin            | 1.1 mg/dL |
| Direct bilirubin           | 0.2 mg/dL |
| Aspartate aminotransferase | 72 U/L    |
| Alanine aminotransferase   | 61 U/L    |
| Alkaline phosphatase       | 110 U/L   |
| Smooth muscle antibody     | Negative  |

A liver biopsy is performed and demonstrates macrovesicular steatosis and necrotic hepatocytes, in addition to centrilobular zone fatty accumulation.

Which of the following is the most likely diagnosis in this patient?

- (A) Nonalcoholic steatohepatitis
- (B) Autoimmune hepatitis
- (C) Alcoholic hepatitis
- (D) Cholelithiasis

**The answer is A: Nonalcoholic steatohepatitis.** The patient in this question is presenting in an asymptomatic state, but has elevated AST, ALT, and alkaline phosphatase levels on laboratory testing. Given her history of hyperlipidemia, diabetes, and obesity, she likely has hepatomegaly and transaminitis secondary to underlying nonalcoholic steatohepatitis (NASH). The histology is further confirmation of this diagnosis given the macrovesicular steatosis and centrilobular zone fatty accumulation findings. (C) Of note, alcoholic hepatitis can present with similar histologic findings, so it cannot be distinguished from NASH solely on pathology. However, this patient denies alcohol use. (B) This

patient has a negative smooth muscle antibody, making autoimmune hepatitis unlikely to be the diagnosis. **(D)** This patient is asymptomatic and does not report any symptoms consistent with cholelithiasis. Even though cholelithiasis can be asymptomatic, the history and pathologic findings in this patient support a diagnosis of NASH.

44

A 21-year-old man presents with flatulence, abdominal pain, and diarrhea for the last 2 years. He has noticed that these symptoms occur after drinking milk or eating yogurt. The diarrhea is nonbloody, watery, and explosive. The patient denies fever, chills, or weight loss. Physical examination is unremarkable.

Which of the following is the best next step in the diagnostic workup of this patient?

- (A)** Acid steatocrit testing
- (B)** Hydrogen breath test
- (C)** Blood cultures
- (D)** Intestinal biopsy

**The answer is B: Hydrogen breath test.** The patient in this question is presenting with classic findings associated with lactose intolerance, a condition in which individuals have insufficient levels of lactase. Lactase is an enzyme that breaks down lactose into glucose and galactose, permitting carbohydrate absorption. If patients are unable to hydrolyze lactose, they develop diarrhea, bloating, and flatulence. The most accurate test is the hydrogen breath test, in which the hydrogen level is measured in one's breath after lactose ingestion. If the lactose cannot be digested, enteric bacteria metabolize it and produce hydrogen that is detected in the test. **(A)** Acid steatocrit testing evaluates for *fat malabsorption*; however, lactose intolerance involves *carbohydrate* malabsorption. **(C)** The patient in this question is not febrile and is not showing signs of infection, so blood cultures are not warranted. **(D)** Intestinal biopsy is sometimes performed after hydrogen breath test confirms elevated hydrogen levels. However, this is not the best initial step in diagnosis.

45

A 59-year-old man with a history of hypertension presents with a 2-month history of weight loss (9.1 kg (20 lb)), malaise, and "yellow skin." The patient denies any abdominal pain. He drinks alcohol socially (three beers per week on average) and has never used illicit drugs. He has a temperature of 36.8°C, blood pressure of 124/90 mmHg, heart rate of 96 beats per minute, and a respiratory rate of 18 breaths per minute. Physical examination reveals jaundice, but no hepatomegaly or abdominal tenderness. Laboratory results reveal a severely elevated alkaline phosphatase (910 U/L) and negative anti-mitochondrial antibodies.



Which of the following is the most likely diagnosis in this patient?

- (A) Primary biliary cirrhosis
- (B) Biliary obstruction secondary to malignancy
- (C) Biliary obstruction secondary to gallstone
- (D) Chronic viral hepatitis infection

**The answer is B: Biliary obstruction secondary to malignancy.** The patient in this question is presenting with a severely elevated alkaline phosphatase in the setting of weight loss, jaundice, and malaise. Elevated alkaline phosphatase indicates obstruction, and given the systemic symptoms of weight loss and malaise, the most likely diagnosis is malignancy causing biliary obstruction, specifically pancreatic adenocarcinoma. *Remember:* the combination of weight loss, painless jaundice, and elevated alkaline phosphatase is highly suggestive of pancreatic cancer! (A) This patient presents with a negative anti-mitochondrial antibody, making primary biliary cirrhosis highly unlikely. (C) Biliary obstruction secondary to gallstones (choledocholithiasis) can present with similar laboratory values (elevated alkaline phosphatase) but usually is accompanied by right upper quadrant pain (not painless jaundice like this patient). (D) Chronic viral hepatitis would not solely elevate the alkaline phosphatase levels; you would also expect elevated aminotransferases. Furthermore, there is no history of hepatitis B or C in this patient's history.

46

A 52-year-old woman presents for her annual physical examination. Her past medical history is significant for hypertension and diabetes mellitus type 2. She endorses smoking two packs of cigarettes per day for the past 18 years. Her vital signs are stable and her physical examination is unremarkable. She receives a colonoscopy that demonstrates multiple diverticular outpouchings. The patient is very concerned and has plenty of questions about the conditions.

Which of the following recommendations should be offered to this patient in the setting of her newly diagnosed condition?

- (A) Smoking cessation
- (B) Prophylactic broad-spectrum antibiotics
- (C) Elective surgical resection
- (D) Increase daily fiber intake

**The answer is D: Increase daily fiber intake.** This patient has multiple diverticula on colonoscopy. Her diverticulosis is currently asymptomatic, but symptomatic diverticulosis can present with abdominal pain, constipation, and painless rectal bleeding. The only recommendation at this stage of the patient's diverticular disease is dietary modification, specifically to increase her daily fiber intake. This generates bulky stools that decrease the likelihood of developing more diverticula. (A) Smoking cessation should always be

recommended to any patient. However, research has not shown that this improves diverticulosis. **(B)** Antibiotics are the treatment of choice in *diverticulitis* that is uncomplicated; however, diverticulitis is associated with fever and leukocytosis, neither of which this patient has. **(C)** Surgery is recommended in complications of diverticular disease, including bleeding or perforation. This patient has asymptomatic diverticulosis and should not be offered surgery.

47

A 43-year-old woman presents with jaundice, right upper quadrant pain, and bothersome pruritus for the past 6 months. Her past medical history is significant for asthma and she only takes inhaled albuterol as needed. Laboratory testing reveals positive anti-mitochondrial antibodies and the patient is diagnosed with primary biliary cirrhosis.

Which of the following is the best initial treatment for this patient?

- (A)** Liver transplantation
- (B)** High-dose steroids
- (C)** Biliary stent placement
- (D)** Ursodeoxycholic acid

**The answer is D: Ursodeoxycholic acid.** This patient has been diagnosed with primary biliary cirrhosis (PBC) as indicated by positive anti-mitochondrial antibodies, jaundice, right upper quadrant pain, and pruritus. PBC is a chronic autoimmune disease of the liver that is associated with intrahepatic duct destruction and cholestasis. The initial drug of choice is ursodeoxycholic acid because it not only reduces cholestasis and improves symptoms but it also has been shown to slow disease progression and therefore increases the time before a liver transplant is needed. **(A)** Liver transplantation is the only curative treatment in PBC; however, this is only an option once the disease has evolved to a cirrhotic state. **(B, C)** Neither high-dose steroids nor biliary stent placement has been shown to be effective in the treatment of PBC mainly because biliary stents do not affect intrahepatic bile ducts that are involved in the disease.

48

A 37-year-old man presents with abdominal pain, mild nausea, and “dark stools.” The patient reports that over the past 6 months he has noticed abdominal pain that is only alleviated by eating. He has gained 6.8 kg (15 lb) during this time period. The patient denies alcohol or illicit drug use, but does report headaches for which he takes over-the-counter acetaminophen. Physical examination is unremarkable; however, fecal occult blood test (FOBT) is positive.

Which of the following is the most likely diagnosis?

- (A)** Peptic ulcer disease
- (B)** Diverticulosis
- (C)** Colon cancer
- (D)** Mesenteric ischemia

**The answer is A: Peptic ulcer disease.** This patient is presenting with melena (dark tarry stools) and abdominal pain. Given the patient's history of alleviation of the abdominal pain with food, it is likely that his symptoms and GI bleeding are secondary to peptic ulcer disease (PUD), specifically duodenal ulcers. Duodenal ulcers are associated with weight gain and gastric ulcers are associated with weight loss. Furthermore, duodenal ulcers and gastric ulcers are both most commonly caused by *H. pylori* infections, but duodenal ulcers are almost entirely (greater than 95%) to be linked to *H. pylori*. Of note, PUD is the most common cause of upper GI bleeding. Diagnosis requires upper endoscopy. **(B)** Diverticulosis is usually asymptomatic; however, if it is associated with GI bleeding, it is typically bright red bleeding. **(C)** Colon cancer should always be considered, but this is a young patient and he does not present with weight loss. Similar to diverticulosis, colon cancer would present with bright red blood per rectum, unless it is a slow, right-sided GI bleed, which can be maroon colored or melenotic. **(D)** Mesenteric ischemia is accompanied by abdominal pain that is worse with eating. However, this patient's abdominal pain improves with eating (making duodenal peptic ulcer disease the most likely diagnosis).

49

A 47-year-old man with a history of chronic viral hepatitis C infection is brought in by his partner for vomiting blood over the past 2 hours. He is unarousable on physical examination and he has a temperature of 36.8°C, blood pressure of 124/90 mmHg, heart rate of 96 beats per minute, and a respiratory rate of 18 breaths per minute. While being examined, the patient begins to vomit a large amount of blood.

In addition to normal saline administration, which of the following is the best next step in management of this patient?

- (A)** Upper GI endoscopy
- (B)** Abdominal CT scan
- (C)** Endotracheal intubation
- (D)** Octreotide

**The answer is C: Endotracheal intubation.** The patient in this question is presenting with unrelenting hematemesis, and given his history of chronic hepatitis C infection, the bleeding is likely secondary to esophageal variceal hemorrhage. This patient is hemodynamically unstable and is continuing to vomit blood. In this situation, the ABCs take precedence; since he has an elevated risk of aspiration from a depressed level of consciousness and ongoing hematemesis, the critical next step to perform (in addition to ample fluid administration) is endotracheal intubation to secure his airway (which is already compromised). **(A)** An upper GI endoscopy is definitely warranted in this case to locate and stop the variceal bleeding; however, this should only be performed after the patient is stabilized. **(B)** Abdominal CT scan is not indicated with GI bleeding. **(D)** Octreotide (a somatostatin analog) is an inhibitory

hormone that leads to vasoconstriction of portal circulation and therefore would be beneficial in this patient. However, stabilization and securing an airway takes precedence in management.

**50** A 27-year-old woman presents with abdominal pain, bloody diarrhea, and nausea for the past 6 weeks. She has lost 4.5 kg (10 lb) over this time period. She has an insignificant past medical history and denies alcohol or illicit drug use. She has a temperature of 38.7°C, blood pressure of 80/48 mmHg, heart rate of 124 beats per minute, and a respiratory rate of 18 breaths per minute. Physical examination demonstrates abdominal distention and tenderness to palpation in all four quadrants. The patient has diminished bowel sounds. Rectal examination is performed and gross blood mixed with mucous is appreciated. The patient's leukocyte count is severely elevated at 28,000/mm<sup>3</sup>.

Which of the following is the initial test of choice in the diagnostic workup of this patient's suspected condition?

- (A) Abdominal ultrasound
- (B) Abdominal x-ray
- (C) Emergent paracentesis
- (D) Colonoscopy

**The answer is B: Abdominal x-ray.** This patient is demonstrating signs and symptoms consistent with inflammatory bowel disease, likely ulcerative colitis (abdominal pain, bloody diarrhea, nausea). She is hemodynamically unstable and has hypotension, tachycardia, leukocytosis, and fever. This presentation is suspicious for toxic megacolon, which is associated with a high mortality rate. To diagnose toxic megacolon, there must be hemodynamic instability, leukocytosis and/or anemia, and signs of colonic distention on abdominal x-ray (colon must be dilated >6 cm). (A, C, D) These are not helpful in diagnosing toxic megacolon. In fact, colonoscopy can be harmful due to its risk for colonic perforation.

## Endocrine and Metabolic Disorders

1

A 37-year-old woman presents with several episodes of anxiety, sweating, and palpitations. She has a blood pressure of 170/110 mmHg and her pulse is 76 beats per minute. The patient recalls being told that she has a “persistently elevated calcium level.” Physical examination reveals a 3.5-cm nonmobile, hard, nontender thyroid nodule. Laboratory results are significant for elevated calcium and parathyroid hormone levels. A fine-needle aspiration biopsy of the thyroid nodule was performed and shows malignant cells.

Which of the following is most likely to be elevated in this patient?

- (A) Thyroglobulin
- (B) Calcitonin
- (C) Alkaline phosphatase
- (D) Erythrocyte sedimentation rate

**The answer is B: Calcitonin.** The patient in this question likely has multiple endocrine neoplasia (MEN) type 2A, also known as Sipple syndrome. The combination of parathyroid hyperplasia, symptoms consistent with pheochromocytoma, and a malignant thyroid nodule makes this the correct answer. The thyroid cancer found in MEN type 2A is medullary carcinoma, which produces calcitonin. (A) Thyroglobulin is used by the thyroid gland to produce T4 and T3. Thyroglobulin levels in the blood are also used as a tumor marker, particularly for papillary or follicular thyroid cancer. Thyroglobulin is not produced in anaplastic or medullary thyroid carcinoma. (C) Alkaline Phosphatase is elevated in several different clinical scenarios, including bile duct obstruction, osteoblastic activity resulting in active bone formation (Paget disease of the bone), and secondary hyperparathyroidism (often from decreased gut absorption of calcium from chronic renal disease). Although the patient in this question has parathyroid hyperplasia, her increased calcium levels would establish the diagnosis of primary hyperparathyroidism (rather than secondary hyperparathyroidism in which you would expect decreased calcium levels). (D) Erythrocyte sedimentation rate (ESR) is a

nonspecific measurement of inflammation. Patients with subacute thyroiditis can have an elevated ESR, but you would expect an exquisitely tender thyroid.

- 2** A 21-year-old woman presents with fatigue that has been present for 6 months. History reveals a diagnosis of asthma and chronic rhinosinusitis that are well controlled with albuterol and fluticasone nasal spray. The patient denies drugs, alcohol, or sexual activity. She has a temperature of 37°C, blood pressure of 120/80 mmHg, heart rate of 75 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 100% on room air. Physical examination reveals dental erosions and the patient refuses to take her hands out of her pockets. Laboratory studies reveal the following.

|                    |                                       |
|--------------------|---------------------------------------|
| Sodium             | 137 mEq/L                             |
| Potassium          | 2.2 mEq/L                             |
| Chloride           | 87 mEq/L                              |
| Bicarbonate        | 39 mEq/L                              |
| Urine chloride     | 12 mEq/L (normal range, 80–250 mEq/L) |
| Arterial blood gas |                                       |
| pH                 | 7.51                                  |

Based on these findings, what is the most likely diagnosis?

- (A) Diuretic abuse
- (B) Surreptitious vomiting
- (C) Diabetic ketoacidosis
- (D) Primary hyperaldosteronism

**The answer is B: Surreptitious vomiting.** The patient in this question has the diagnosis of surreptitious vomiting. The combination of dental erosions, metabolic alkalosis, and hypochloremia makes this the correct answer. The patient also has a low urine chloride concentration. (A) Diuretic abuse should definitely be considered in this clinical scenario as patients with diuretic abuse also present with hypokalemia and metabolic alkalosis; however, their urine chloride concentrations are usually high. (C) Diabetic ketoacidosis (DKA) results in metabolic acidosis (with anion gap), not metabolic alkalosis. (D) Primary hyperaldosteronism is caused by adrenal hyperplasia or by an aldosterone-secreting adrenal adenoma. This results in hypertension, hypokalemia,

metabolic alkalosis, and low plasma renin. The patient in this question is normotensive, making this diagnosis unlikely.



A 74-year-old man with a history of New York Heart Association class III congestive heart failure presents with vague abdominal pain that has inconsistently responded to acetaminophen. He has a temperature of 37°C, blood pressure of 172/88 mmHg, heart rate of 75 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation of 99% on room air. Physical examination reveals abdominal pain on deep palpation in all four quadrants. Laboratory studies reveal a serum sodium of 148 mEq/L, serum potassium of 2.8 mEq/L, and an increased plasma aldosterone to plasma renin activity ratio of 51 (normal range, 0.9 to 20). CT scan shows an incidental left adrenal mass. The patient is deemed a poor surgical candidate due to his cardiovascular state.

Which of the following is the next best step in management?

- (A) Hydrochlorothiazide
- (B) Phenoxybenzamine
- (C) Spironolactone
- (D) Verapamil

**The answer is C: Spironolactone.** The patient in question has primary hyperaldosteronism, as evidenced by hypertension, hypokalemia, and an adrenal mass on CT scan. Although this patient has a unilateral adrenal adenoma, patients with primary hyperaldosteronism can also have bilateral adrenal hyperplasia. Clues to diagnosis include an elevated plasma aldosterone to plasma renin activity ratio ( $>20$ ). The increased aldosterone levels act via negative inhibition to decrease renin levels. CT scan can distinguish a unilateral adenoma from bilateral adrenal hyperplasia. Although surgery is preferred for patients with a unilateral adrenal adenoma, medical therapy is the preferred route for patients with bilateral adrenal hyperplasia or those with unilateral adrenal adenoma who are poor surgical candidates. Spironolactone is an aldosterone antagonist that also acts as an androgen receptor antagonist. Side effects include gynecomastia in men and menstrual irregularities in women among others. If side effects are a concern for the patient, eplerenone is an alternative treatment. Eplerenone is a selective mineralocorticoid antagonist, but with low affinity for androgen receptors. (A) Hydrochlorothiazide is indeed recommended for blood pressure control in primary hyperaldosteronism if aldosterone antagonist therapy is insufficient. However, it is not the first drug that should be administered. (B) Phenoxybenzamine is a nonspecific and irreversible  $\alpha$ -blocker used in the medical management of pheochromocytoma. (D) Verapamil is another antihypertensive used in some patients, but is not first-line medical therapy in a patient with primary hyperaldosteronism.

4

A 36-year-old woman with a history of Graves disease presents with perioral numbness and muscle cramps for the last 2 weeks. She underwent a thyroidectomy 2 months ago for a large goiter that was beginning to compress her trachea. She has never had these symptoms before and her family history is insignificant. Physical examination is unremarkable and laboratory studies reveal the following.

|                     |                    |
|---------------------|--------------------|
| Sodium              | 138 mEq/L          |
| Potassium           | 4.2 mEq/L          |
| Chloride            | 101 mEq/L          |
| Bicarbonate         | 24 mEq/L           |
| Blood urea nitrogen | 11 mg/dL           |
| Creatinine          | 0.9 mg/dL          |
| Glucose             | 98 mg/dL (fasting) |
| Calcium             | 6.2 mg/dL          |
| Phosphorus          | 5.3 mg/dL          |

Which of the following is associated with her condition?

- (A) Peaked T waves on ECG
- (B) Widening of the QRS complex on ECG
- (C) Prolongation of the QT interval on ECG
- (D) Shortened QT interval on ECG

**The answer is C: Prolongation of the QT interval on ECG.** The patient in this question presents with signs and symptoms of hypocalcemia (perioral numbness and muscle cramps). Other signs of hypocalcemia include tetany, carpopedal spasms, and neuromuscular irritability. The patient has primary hypoparathyroidism as evidenced by low serum calcium levels and elevated phosphorus levels. Chronic renal failure can also produce low serum calcium levels and elevated phosphorus levels, but this patient has normal BUN and creatinine levels, so she does not show signs of kidney failure. On ECG, hypocalcemia presents as a prolongation of the QT interval. (A) Peaked T waves on ECG are seen with hyperkalemia. (B) Widening of the QRS complex is also seen with hyperkalemia, but can be seen with bundle branch block as well. (D) Shortened QT interval on ECG is seen with hypercalcemia.



- 5 An obese 32-year-old woman with a history of gastroesophageal reflux disease (GERD) presents with amenorrhea for the past year. Review of systems is unremarkable. She has 3 children and denies tobacco, alcohol, or drug use. She has a temperature of 37°C, blood pressure of 120/80 mmHg, heart rate of 75 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 100% on room air. Visual field testing reveals no abnormality and her pregnancy test is negative. Laboratory studies reveal a serum prolactin level of 108 ng/mL. MRI of the pituitary gland confirms a 5.5-mm pituitary adenoma.

Which of the following is the next best step in management?

- (A) Treatment with bromocriptine
- (B) Estrogen replacement therapy
- (C) Surgery
- (D) Serial prolactin levels and close observation

**The answer is A: Treatment with bromocriptine.** The patient in this question presents with symptoms and laboratory values consistent with a prolactinoma. The presence of amenorrhea and galactorrhea in females and hypogonadism in males are classic symptoms for a prolactinoma. An adenoma of the pituitary gland less than 10 mm is called a microadenoma, which does not usually have a mass effect that would affect other pituitary hormones. The first-line treatment for all prolactinomas remains dopamine agonists such as bromocriptine and cabergoline. These agents often decrease prolactin levels to the normal range and shrink the tumor. Dopamine agonists inhibit secretion of prolactin from the anterior lobe of the pituitary gland. (B) Estrogen replacement therapy is often given to patients who experience intolerable side effects from the use of dopamine agonists, but is not first-line treatment. (C) Surgery is often indicated for those patients with prolactinoma who have visual field defects that do not improve quickly after medical treatment with dopamine agonists. Surgery is also an option for those patients who do not respond to dopamine agonists. (D) Serial prolactin levels and close observation remain an option for asymptomatic patients with prolactinoma given the slow growth (however, this patient presents with amenorrhea).

- 6 A 64-year-old man with a history of hypertension and a 30-pack-year smoking history presents with unrelenting abdominal pain and constipation. He also endorses nausea and his wife reports that he has exhibited subtle signs of mental deterioration. He has a temperature of 36.8°C, blood pressure of 118/72 mmHg, heart rate of 98 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation of 96%

on room air. Physical examination is unremarkable and laboratory studies reveal the following.

|                           |                                          |
|---------------------------|------------------------------------------|
| Calcium                   | 15.1 mg/dL                               |
| Albumin                   | 3.9 g/dL                                 |
| Serum parathyroid hormone | 8 pg/mL                                  |
| 1,25-dihydroxyvitamin D   | 13 pm/mL (normal range, 15.9–55.6 pg/mL) |

What additional laboratory value do you expect to find with this patient's condition?

- (A) Increased angiotensin-converting enzyme (ACE) blood levels
- (B) Decreased interleukin-6 levels
- (C) Decreased urine calcium levels
- (D) Increased levels of parathyroid hormone–related protein

**The answer is D: Increased levels of parathyroid hormone–related protein.**

The patient in this question presents with classic features of hypercalcemia (polyuria, nausea, vomiting, polydipsia, constipation, and cognitive dysfunction). His serum calcium is elevated with a suppressed serum parathyroid hormone (PTH) level. In addition, the history of extensive smoking gives an important clue that hypercalcemia of malignancy should be highly considered here. With hypercalcemia of malignancy, serum calcium levels are much more elevated than in patients with primary hyperparathyroidism (the most common cause of hypercalcemia, but in this case not the diagnosis given that serum PTH is suppressed with this patient). (B) In hypercalcemia of malignancy, osteolytic metastases contribute to the markedly elevated calcium level, but you would also expect secretion of parathyroid hormone–related protein (PTH-rP), in addition to increased interleukin-6 levels. (A) Increased angiotensin-converting enzyme (ACE) blood levels is often seen in sarcoidosis; however, this patient has low 1,25-dihydroxyvitamin D levels and you would expect elevated levels in sarcoidosis due to the increased conversion in granulomatous tissue. Also, calcium is usually not as high in sarcoidosis. (C) Decreased urine calcium levels would be found in another cause of hypercalcemia called familial hypercalcemia hypocalciuria; however, this would be accompanied by high to normal PTH levels (and this patient has suppressed serum PTH levels).



7 A 32-year-old woman with a history of endometriosis presents with weight loss, diarrhea, and increased appetite for the past 6 weeks. She has a temperature of 37°C, blood pressure of 132/88 mmHg, heart rate of 75 beats per minute, respiratory rate of 18 breaths per minute, and

oxygen saturation of 99% on room air. Physical examination reveals a diffusely large, nontender thyroid gland in addition to the findings seen in the photo below (*Figure 5-1*). Laboratory studies confirm the diagnosis and the patient opts for treatment with methimazole.



**Figure 5-1**

Which of the following adverse effects is important to inform the patient of before beginning treatment with this medication?

- (A) Hypocalcemia
- (B) Acute liver failure
- (C) Agranulocytosis
- (D) Vasculitis

**The answer is C: Agranulocytosis.** The patient in this question has been diagnosed with Graves disease and demonstrates exophthalmos and lid retraction. In addition to methimazole, propylthiouracil is another antithyroid drug that can be used in place of radioactive iodine ablation or thyroidectomy. There are several side effects of propylthiouracil and methimazole, several of which are shared by both drugs and some that are unique to each one. Side effects that are shared by both include skin rash, arthralgias, hepatotoxicity, and agranulocytosis. Methimazole can cause jaundice and is teratogenic in the first trimester. (B, D) Propylthiouracil (PTU) can cause vasculitis and is not preferred over methimazole since it carries a risk of acute liver failure. Of note, PTU is preferred during pregnancy. (A) Hypocalcemia is indeed an adverse effect from thyroidectomy, but the patient in this question opted for medical management over surgery.

**8**

A 28-year-old man with a history of type 1 diabetes presents with polydipsia and polyuria for the last 5 weeks. The patient reports that his blood glucose levels have been well controlled on his current insulin regimen. The patient denies tobacco, alcohol, or drug use and has no other past medical history. He has a temperature of 36.8°C, blood pressure of 114/68 mmHg, heart rate of 96 beats per minute, respiratory rate of 16 breaths per minute,

and oxygen saturation of 98% on room air. The patient reports that he has fasted for the visit and laboratory results reveal the following.

|                                                |             |
|------------------------------------------------|-------------|
| Sodium                                         | 147 mEq/L   |
| Potassium                                      | 3.8 mEq/L   |
| Chloride                                       | 104 mEq/L   |
| Bicarbonate                                    | 28 mEq/L    |
| Blood urea nitrogen                            | 16 mg/dL    |
| Creatinine                                     | 1.1 mg/dL   |
| Glucose                                        | 96 mg/dL    |
| Serum osmolality before water deprivation test | 310 mOsm/kg |
| Urine osmolality before water deprivation test | 98 mOsm/kg  |
| Serum osmolality after water deprivation test  | 322 mOsm/kg |
| Urine osmolality after water deprivation test  | 101 mOsm/kg |

Desmopressin was administered and 30 minutes later the urine osmolality is 432 mOsm/kg.

Which of the following is this patient's diagnosis?

- (A) Primary polydipsia
- (B) Central diabetes insipidus
- (C) Nephrogenic diabetes insipidus
- (D) Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

**The answer is (B): Central diabetes insipidus.** The patient in this question presents with polyuria and polydipsia with a normal serum glucose level. Given the patient's hypernatremia, low urine osmolality, and elevated serum osmolality, the patient likely has diabetes insipidus (DI) and it now remains to distinguish between central and nephrogenic DI.

(A) Primary polydipsia is not the answer here because in primary polydipsia you would expect hyponatremia given that the increased water consumption in primary polydipsia overwhelms the capability of the kidneys to excrete the water. (D) SIADH is incorrect for the same reason—you would expect hyponatremia and this patient has hypernatremia (sodium >145 mEq/L). Central DI occurs when the pituitary gland does not secrete sufficient ADH. Nephrogenic DI occurs when the nephrons themselves show resistance to ADH (but ADH levels will be normal because the pituitary gland is functionally intact). In nailing the diagnosis, the patient must first engage in a water deprivation test for at least 2 hours. If the urine osmolality is >600 mOsm/kg at the conclusion of the test,

then the diagnosis is likely primary polydipsia since the patient is able to concentrate urine without water intake. If the urine is still dilute ( $<600$  mOsm/kg) at the end of the water deprivation test, then desmopressin (synthetic vasopressin) is administered and urine osmolality is monitored. If urine osmolality increases, then this proves that pituitary secretion of ADH is deficient and central DI is diagnosed. Nephrogenic DI will have negligible change in urine osmolality since the problem is renal pathology (not the amount of ADH). The patient in this question has a urine osmolality that increased about 400% after desmopressin, establishing the diagnosis as central DI.



A 72-year-old woman presents with bone pain and tenderness in her lower extremities and left clavicle. Review of her chart reveals chronic bone marrow fibrosis with increased bone remodeling, in addition to several episodes of kidney stones (specifically calcium oxalate). Physical examination reveals tenderness to palpation on her lower legs and left midclavicle. Laboratory studies reveal elevated calcium, decreased phosphate, and elevated parathyroid hormone (PTH). X-ray reveals the following (*Figure 5-2*).



**Figure 5-2**

Which of the following is the diagnosis?

- (A) Paget disease of the bone
- (B) Osteomalacia
- (C) Osteoporosis
- (D) Osteitis fibrosa cystica

**The answer is D: Osteitis fibrosa cystica.** The patient in this question has hyperparathyroidism (elevated PTH) and is showing clinical symptoms for osteitis fibrosa cystica, a disease in which cystic bone spaces are filled with brown fibrous tissue. This disease is associated with hyperparathyroidism because PTH first acts on osteocytes and then on osteoclasts, causing calcium to be resorbed from the bone matrix and available in the blood stream (hypercalcemia). PTH also causes decreased phosphate reabsorption in the nephron, which causes decreased blood phosphate levels (hypophosphatemia). Hypercalciuria is yet another sign of hyperparathyroidism, which leads to the formation of calcium oxalate stones. The above figure shows osteosclerosis with greater density at the endplates (rugger jersey spine), which can be seen with hyperparathyroidism.

(A, C) Paget disease of the bone also causes bone pain and involves disorganized bone remodeling, but this disease usually causes misshapen bones and fractures and is typically localized to only a few bones in the body, in contrast with osteoporosis in which typically all the bones in the body are affected. Furthermore, laboratory studies are critical for nailing the diagnosis, since Paget disease of the bone and osteoporosis do not cause changes in calcium, phosphate, and PTH levels (although Paget disease is associated with increased alkaline phosphatase). (B) Osteomalacia involves defective bone mineralization due to vitamin D deficiency in adults, causing decreased calcium levels, which subsequently causes PTH to increase. With the increased secretion of PTH, serum phosphate levels decrease.

**10** A 48-year-old woman presents with weight gain, easy bruisability, and muscle weakness. She has a 30-pack-year history of smoking. She presents with a temperature of 36.8°C, blood pressure of 144/92 mmHg, heart rate of 96 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 98% on room air. Physical examination reveals the finding seen in the photo (*Figure 5-3*). Laboratory studies are significant for a fasting blood glucose of 310 mg/dL, a 24-hour urine cortisol level of 1,200 µg (normal range, 10 to 100 µg), and a plasma ACTH of 126 pg/mL (normal range, 10 to 60 pg/mL). Twenty-four-hour urine cortisol level is 1,184 µg after high-dose dexamethasone is administered.



**Figure 5-3**

Which of the following is the cause of the patient's symptoms and laboratory findings?

- (A) Exogenous steroids
- (B) Adrenocortical adenoma
- (C) Ectopic ACTH-producing tumor
- (D) Cushing disease

**The answer is C: Ectopic ACTH-producing tumor.** The patient in this question is presenting with typical symptoms of Cushing syndrome. In addition to weight gain, easy bruisability, and muscle weakness, symptoms include moon facies, truncal obesity, buffalo hump, hyperglycemia, osteoporosis, amenorrhea, and hypertension. Cushing syndrome by definition only signifies increased cortisol levels, so there must be a workup to determine the etiology of the disorder. One must first diagnose Cushing syndrome by initially screening with a 24-hour urine cortisol level. The vast majority of patients with Cushing syndrome have levels greater than 90  $\mu\text{g}/24$  hours. Once the diagnosis of Cushing syndrome has been made, the etiology must then be determined by measuring plasma ACTH level (elevated ACTH is considered greater than 20  $\text{pg}/\text{mL}$ ). (A) The most common cause of Cushing syndrome is exogenous steroids; however, this will have a low ACTH level due to the steroids negatively inhibiting secretion of ACTH from the pituitary. (B) Likewise, adrenal-related causes of Cushing syndrome such as adrenocortical adenoma will have a decreased ACTH level. Our patient, on the other hand, presents with an elevated ACTH level and so then next step is to distinguish between Cushing disease (increased ACTH secretion

from a pituitary adenoma) and ectopic ACTH production, sometimes seen in small cell lung cancer. **(D)** High-dose dexamethasone will normally suppress urinary cortisol or serum cortisol levels in Cushing disease, but will not suppress cortisol levels in ectopic ACTH production. In this patient, 24-hour urine cortisol levels were not adequately suppressed (defined as suppressing cortisol levels by at least 50%), so ectopic ACTH production (likely small cell lung cancer given the patient's smoking history) is the diagnosis.

- 11** A 28-year-old woman presenting with diarrhea, sweating, palpitations, and anxiety is found to have a diminished TSH (0.1  $\mu\text{U/mL}$ ) and an elevated free T4 (32  $\mu\text{g/dL}$ ).

What is the next best step in management?

- (A)** Thyroglobulin
- (B)** Radioactive iodine uptake (RAIU) scan
- (C)** Thyroid antibodies
- (D)** A fine-needle aspiration (FNA) biopsy

**The answer is B: Radioactive iodine uptake (RAIU) scan.** The patient is presenting clinically with hyperthyroidism and laboratory values (decreased TSH and elevated free T4) confirm a diagnosis of *primary* hyperthyroidism. However, there are several etiologies of primary hyperthyroidism, including Graves disease (the most common), toxic multinodular goiter, functioning adenoma, and other rare causes (thyroiditis, struma ovarii, thyrotoxicosis factitia). The next best step to distinguish these causes from each other is an RAIU scan. If the RAIU scan reveals *diffuse* iodine uptake, then it is Graves (if it is *homogeneously* diffuse) or toxic multinodular goiter (if it is *heterogeneously* diffuse). If the RAIU scan reveals *focal* iodine uptake, it is likely a functioning adenoma. **(B)** If the RAIU scan reveals no iodine uptake, then serum thyroglobulin should be ordered as an increased level indicates thyroiditis, struma ovarii, or iodine load and a decreased level indicates thyrotoxicosis factitia. **(C)** Thyroid antibodies are a good test to order, but this is not the next best step in working up primary hyperthyroidism. Antithyroid peroxidase (anti-TPO) antibodies are seen in Hashimoto disease, and TSH receptor antibodies are seen in Graves disease. **(D)** FNA biopsy is typically performed in the workup of a thyroid nodule, particularly after TSH returns normal or RAIU confirms a cold nonfunctional nodule, in order to rule in/out malignancy.

- 12** A 58-year-old man with a 50-pack-year smoking history presents with forgetfulness. He constantly forgets to lock the door when he leaves for work and locked his keys in his car two times last week. He presents with a temperature of 36.8°C, blood pressure of 134/86 mmHg, heart rate of 96 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 96% on room air.



Physical examination is unremarkable and laboratory results reveal the following.

|                     |                |
|---------------------|----------------|
| Sodium              | 128 mEq/L      |
| Potassium           | 3.8 mEq/L      |
| Chloride            | 99 mEq/L       |
| Bicarbonate         | 24 mEq/L       |
| Blood urea nitrogen | 11 mg/dL       |
| Creatinine          | 0.9 mg/dL      |
| Serum osmolality    | 242 mOsm/kg    |
| Urine osmolality    | 476 mOsm/kg    |
| Urine sodium        | 42 mEq/L       |
| TSH                 | 3.8 $\mu$ U/mL |

Which of the following is the best subsequent step in managing this condition?

- (A) Normal saline
- (B) Fluid restriction
- (C) Hypertonic saline
- (D) Dexamethasone

**The answer is B: Fluid restriction.** This patient is presenting with hyponatremia and the etiology must be determined before management proceeds. Given the low serum osmolality, high urine osmolality, and high urine sodium, this patient likely has SIADH in the context of normal creatinine, potassium, and thyroid laboratory values. Other causes of decreased serum osmolality include primary polydipsia and malnutrition, but these would cause low urine osmolality (in contrast with our patient). Given the patient's smoking history, he likely has lung cancer (small cell lung cancer) which is a common malignancy causing SIADH.

This question goes beyond diagnosing SIADH though; it asks for the appropriate management. In SIADH, treatment depends on severity of symptoms. In an asymptomatic or mildly symptomatic (forgetfulness, gait changes) patient, the treatment is fluid restriction to less than 800 mL/d. A loop diuretic can be administered as well if the urine osmolality is greater than  $2\times$  the serum osmolality. (C) Hypertonic saline is given as the first treatment in SIADH if

the patient presents with moderate (confusion, lethargy) or severe (seizures, comatose) state. Our patient is clearly demonstrating mild symptoms so fluid restriction is the next best step in management. (A) Normal saline would worsen the hyponatremia here since it ultimately leads to sodium chloride excretion; however, in SIADH, the amplified ADH response would further concentrate the urine and dilute the blood and theoretically worsen the hyponatremia. In addition, administering a fluid with lower osmolality than the urine will cause net reabsorption of water. (D) Dexamethasone is a steroid and can be used in many inflammatory conditions, but is not useful in treating hyponatremia caused by SIADH.

13

A 34-year-old woman with an insignificant past medical history presents with unrelenting headaches for the past 2 weeks. She has a temperature of 36.8°C, blood pressure of 168/102 mmHg, heart rate of 96 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 98% on room air. One year prior to this episode, her recorded blood pressure was 134/86 mmHg. Physical examination was unremarkable except for a faint bruit on the left side just inferior to the costal margin. Laboratory studies reveal a serum sodium of 148 mEq/L and a serum potassium of 2.8 mEq/L. Magnetic resonance angiography (MRA) shows a “string of beads” appearance of the left renal artery.

Which of the following laboratory values do you expect with this condition?

- |   |              |                                          |
|---|--------------|------------------------------------------|
|   | Plasma renin | Plasma aldosterone to plasma renin ratio |
| A | Increased    | Increased                                |
| B | Increased    | Decreased                                |
| C | Decreased    | Increased                                |
| D | Decreased    | Decreased                                |

**The answer is B: Increased plasma renin and decreased plasma aldosterone to plasma renin ratio.** The patient in this question has fibromuscular dysplasia, a condition that commonly affects young women of childbearing age. The patient is presenting with new-onset hypertension along with laboratory values that reflect hyperaldosteronism (hypernatremia and hypokalemia). In this situation, the physical examination finding of a faint bruit inferior to the left costal margin and the “string of beads” MRA finding supports an etiology of *secondary* hyperaldosteronism, specifically fibromuscular dysplasia. Other causes of secondary hyperaldosteronism include renal artery stenosis, chronic renal failure, CHF, cirrhosis, and even nephrotic syndrome. All these conditions have an important characteristic in common: Kidney perception of *low* intravascular volume which upregulates the renin-angiotensin system. (C, D) Decreased plasma renin would be seen in primary hyperaldosteronism (caused by adrenal hyperplasia or an aldosterone-secreting adrenal adenoma) because in these disorders the kidneys perceive high intravascular volume

which downregulates the renin–angiotensin system. (A) The overactive renin–angiotensin system seen in secondary hyperaldosteronism contributes to high plasma renin level and accordingly, a decreased (or sometimes normal) plasma aldosterone to plasma renin ratio.

- 14** A 29-year-old woman presents with heat intolerance, weight loss, and diarrhea. Her past medical history is significant for type 2 diabetes. She has a temperature of 36.8°C, blood pressure of 136/64 mmHg, heart rate of 102 beats per minute, respiratory rate of 20 breaths per minute, and oxygen saturation of 98% on room air. Physical examination is significant for a palpable 3-cm spherical and well-demarcated nodule on the right lobe of her thyroid gland. Her skin is moist. Laboratory studies reveal the following.

|     |                 |
|-----|-----------------|
| TSH | 0.05 $\mu$ U/mL |
| T3  | 276 ng/dL       |
| T4  | 16 $\mu$ g/dL   |

The patient is opposed to surgery and very hesitant to receive medical treatment for the condition. If she opts for no treatment, what is she at risk for developing?

- (A) Thyroid malignancy
- (B) Infiltrative ophthalmopathy
- (C) Atrial fibrillation
- (D) Bone growth

**The answer is C: Atrial fibrillation.** The patient in this question has a toxic thyroid adenoma, a common cause of hyperthyroidism that results in focal hyperplasia of thyroid follicular cells that function independently of regulation by TSH. Although relatively common, it is less common than Graves disease. This question requires the student to not only know the diagnosis, but to also understand the side effects if left untreated. If no treatment is given, patients with hyperthyroidism can develop life-threatening cardiac arrhythmias secondary to the direct action of free thyroid hormone causing an elevated circulatory demand. This increased metabolic state can cause tachycardia, systolic hypertension, and certain tachyarrhythmias like atrial fibrillation. (A) Thyroid malignancy resulting from toxic adenoma of the thyroid gland is exceedingly rare. However, it is important to note that “cold” or nonfunctioning nodules are more concerning for cancer. (B) Infiltrative ophthalmopathy occurs in Graves disease and results from glycosaminoglycans building up in the retro-orbital and extraocular muscles. Graves disease is associated with diffuse enlargement

(goiter) of the thyroid gland and pretibial myxedema. **(D)** Bone growth is the opposite of what one would expect in untreated hyperthyroidism. Rather, rapid bone loss can occur because thyroid hormone acts directly on bone cells, causing osteoclastic bone resorption (and hypercalcemia from the increased calcium release from the bones).

**15** A 53-year-old man with a history of type 2 diabetes presents with swollen legs for the last month. The patient is asymptomatic otherwise. His current medications include a multivitamin and metformin. HbA1c was 7.9% at his annual visit in the previous year. He has a temperature of 36.8°C, blood pressure of 142/78 mmHg, heart rate of 68 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 98% on room air. Physical examination reveals 2+ bilateral pitting edema up to his midtibia region. Laboratory results reveal the following.

|                       |           |
|-----------------------|-----------|
| Sodium                | 142 mEq/L |
| Potassium             | 4.0 mEq/L |
| Chloride              | 99 mEq/L  |
| Bicarbonate           | 22 mEq/L  |
| Blood urea nitrogen   | 41 mg/dL  |
| Creatinine            | 3.1 mg/dL |
| Blood glucose         | 152 mg/dL |
| 24-hour urine protein | 2.9 g/d   |

Which of the following should be administered to reduce the progression of this patient's underlying renal condition?

- (A)** Sulfonylurea
- (B)** Lisinopril
- (C)** Atorvastatin
- (D)** Aspirin

**The answer is B: Lisinopril.** The patient in this question has diabetic nephropathy and macroproteinuria (urine protein excretion greater than 300 mg/d). Diabetic nephropathy first manifests itself through an increased GFR and then microalbuminuria before progressing to macroproteinuria. Strict blood pressure control is the only effective treatment for reducing the progression of diabetic nephropathy. In diabetic patients, the blood pressure goal must be below 130/80 mmHg and ACE inhibitors (Lisinopril) are

the antihypertensive drug of choice to prevent or slow the progression of nephropathy. ACE inhibitors are beneficial for diabetic patients because they slow the decline in GFR by reducing the hyperfiltration occurring at the level of the nephron. Potassium levels must be monitored very carefully in patients taking an ACE inhibitor due to the risk for hyperkalemia. (A) This patient is demonstrating azotemia with a BUN of 41 mg/dL and optimizing blood glucose control with an additional antidiabetic agent (although important with the patient's recent HbA1c level) is not superior to strict blood pressure control in reducing progression of his diabetic nephropathy. (C, D) Lipid control and aspirin are beneficial for reducing the likelihood of coronary heart disease, but has not been shown to be effective in improving diabetic nephropathy.

16

A 73-year-old woman with a history of type 2 diabetes and hypertension presents with rapid breathing, nausea, abdominal pain, and diarrhea. Her blood glucose has been well controlled and a rapid bedside blood glucose test reveals a level of 106 mg/dL. She informs you that 3 weeks ago she was taken off an oral antidiabetic medication due to several episodes of hypoglycemia and started on another oral antidiabetic medication, but she cannot recall the name. She has a temperature of 36.8°C, blood pressure of 120/78 mmHg, heart rate of 96 beats per minute, respiratory rate of 28 breaths per minute, and oxygen saturation of 96% on room air.

Based on clinical history and physical examination, which of the following do you expect on arterial blood gas?

- (A) Metabolic alkalosis
- (B) Respiratory acidosis
- (C) Respiratory alkalosis
- (D) Metabolic acidosis with high anion gap
- (E) Metabolic acidosis with normal anion gap

**The answer is D: Metabolic acidosis with high anion gap.** The patient in this question is presenting with hyperventilation due to an underlying acid-base change. This question tests the student's knowledge of side effects of oral antidiabetic medications. Given the patient's normal blood glucose level, it is very unlikely that she is suffering from DKA; however, she informs you that she recently changed medications and now has abdominal pain and diarrhea. These are likely side effects from metformin (a biguanide medication that inhibits hepatic gluconeogenesis). Given the previous medication caused hypoglycemia, she was likely taking a sulfonylurea (which increases insulin secretion and therefore can cause hypoglycemia). Metformin can cause lactic acidosis, one of the several causes of high anion gap metabolic acidosis (others include methanol, uremia from chronic renal failure, DKA, propylene glycol, isoniazid, ethylene glycol, and salicylates). This would explain her hyperventilation because she is compensating for a low bicarbonate level. Other side

effects of metformin include metallic taste and weight loss. Metformin should not be given in patients with renal insufficiency or liver disease. **A, B, D,** and **E** are other acid–base abnormalities that have completely different etiologies than lactic acidosis. Of note, metabolic acidosis with a normal anion gap is typically associated with chronic diarrhea, renal tubular acidosis (RTA), and ureterosigmoidostomy.

**17** A 53-year-old man with a history of thyroid medullary cancer presents with several episodes of a “racing heart,” palpitations, diaphoresis, and headaches. He has a temperature of 37.8°C, blood pressure of 158/96 mmHg, heart rate of 96 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation of 96% on room air. Urine test reveals small amounts of normetanephrine and metanephrine.

Which of the following, if present in this patient, would establish the diagnosis as multiple endocrine neoplasia (MEN) type 2B?

- (A)** Parathyroid hyperplasia
- (B)** Mucocutaneous neuromas
- (C)** Pituitary adenoma
- (D)** Proptosis

**The answer is B: Mucocutaneous neuromas.** The patient in this question is presenting with signs and symptoms of pheochromocytoma, a neuroendocrine tumor of the adrenal medulla that secretes high amounts of catecholamines. Given that he has a history of thyroid medullary cancer, the MEN syndromes must be considered highly on the differential diagnosis. Both MEN type 2A and MEN type 2B include thyroid medullary cancer and pheochromocytoma. However, only MEN type 2B includes mucocutaneous neuromas

**Table 5-1 Findings in the MEN Syndromes**

| MEN Syndrome         | Distinguishing Characteristics                                                                                                                                                                                       |
|----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MEN type 1 (Wermer)  | <ul style="list-style-type: none"><li>• Parathyroid hyperplasia</li><li>• Pancreatic islet cell tumor</li><li>• Pituitary adenoma</li></ul>                                                                          |
| MEN type 2A (Sipple) | <ul style="list-style-type: none"><li>• Parathyroid hyperplasia</li><li>• Thyroid medullary cancer</li><li>• Pheochromocytoma</li></ul>                                                                              |
| MEN type 2B          | <ul style="list-style-type: none"><li>• Thyroid medullary cancer</li><li>• Pheochromocytoma</li><li>• Mucocutaneous neuromas</li><li>• Marfan-like body habitus</li><li>• Ganglioneuromatosis of the colon</li></ul> |

as one of its characteristic diagnoses. MEN type 2B also is characterized by marfan-like body habitus and ganglioneuromatosis of the colon. **(A)** Parathyroid hyperplasia is seen in MEN type 1 and MEN type 2A, but not in MEN type 2B. **(C)** Pituitary adenoma is seen in MEN type 1, but not in the other MEN syndromes. **(D)** Proptosis is often seen in Graves disease, the most common cause of hyperthyroidism. This information is summarized in *Table 5-1*.

18

A 23-year-old man with a history of type 1 diabetes presents with nausea, vomiting, abdominal pain, and rapid breathing. His girlfriend reports that he has a “nail polish” odor. The symptoms appeared 24 hours ago and have rapidly worsened. Two weeks ago he was treated for pneumonia. He has a temperature of 37.8°C, blood pressure of 92/58 mmHg, heart rate of 104 beats per minute, respiratory rate of 26 breaths per minute, and oxygen saturation of 94% on room air. Physical examination reveals decreased skin turgor, dry axillae and oral mucosa, and low jugular venous pressure. Laboratory results reveal the following.

|                     |                                              |
|---------------------|----------------------------------------------|
| Sodium              | 142 mEq/L                                    |
| Potassium           | 4.0 mEq/L                                    |
| Chloride            | 100 mEq/L                                    |
| Bicarbonate         | 14 mEq/L                                     |
| Blood urea nitrogen | 16 mg/dL                                     |
| Creatinine          | 0.8 mg/dL                                    |
| Glucose             | 620 mg/dL                                    |
| β-hydroxybutyrate   | 8.4 mg/dL (normal range, 0.21 to 2.81 mg/dL) |
| Arterial blood gas  |                                              |
| pH                  | 7.28                                         |

Treatment with IV fluids and insulin is initiated.

Which of the following should NOT be used to monitor response to therapy?

- (A)** Urine ketones via nitroprusside test
- (B)** Serum β-hydroxybutyrate level
- (C)** Serum bicarbonate concentration
- (D)** Serum anion gap

**The answer is A: Urine ketones via nitroprusside test.** The patient in this question presents with signs and symptoms of DKA, a high anion gap metabolic acidosis. It is first important to distinguish DKA from hyperosmolar hyperglycemic state (HHS). These two diseases are distinguishable based on the level of hyperglycemia and the presence of ketoacidosis. In DKA, the serum glucose typically does not exceed 800 mg/dL, in contrast to HHS where the serum glucose usually exceeds 1,000 mg/dL. Furthermore, in HHS there is typically no ketone production and the osmolality can approach 380 mOsm/kg.

**(B)** The preferred way to monitor treatment of DKA with IV fluids and insulin is to directly measure serum  $\beta$ -hydroxybutyrate. **(C, D)** However, given that this approach is not available in all hospitals, one can also monitor response to treatment with serum bicarbonate concentration (to analyze the improvement of metabolic acidosis) and also serum anion gap (to determine if the ketoacidosis is being corrected). Recall that serum anion gap estimates the unmeasured anions in the plasma; in DKA, this is useful information due to the presence of ketoacid anions. Urine ketones via nitroprusside test should not be used to monitor response because during treatment with insulin,  $\beta$ -hydroxybutyrate is converted to acetoacetate. Since nitroprusside measures acetoacetate and acetone (but not  $\beta$ -hydroxybutyrate), a positive nitroprusside test can give the false impression that the ketoacidosis has worsened. Furthermore, given that  $\beta$ -hydroxybutyrate is the predominant ketone in DKA, a serum nitroprusside test can be negative in the presence of moderate to severe ketosis.

**19** A 39-year-old man presents with anxiety, sweating, and palpitations for the last 2 months. He has a blood pressure of 168/112 mmHg and his pulse is 84 beats per minute. The patient is diaphoretic on physical examination. Urine normetanephrine and metanephrine levels are found to be elevated.

Before surgical resection is performed for this condition, what medication must be administered?

- (A)** Atenolol
- (B)** Phenoxybenzamine
- (C)** Lisinopril
- (D)** Clonidine

**The answer is B: Phenoxybenzamine.** The patient in this question is presenting with pheochromocytoma, a catecholamine-secreting neuroendocrine tumor of the medulla of the adrenal glands. Eighty percent of pheochromocytomas are unilateral, 10% are bilateral, and 10% are extra-adrenal. Surgical resection of the pheochromocytoma is the treatment of choice, but the patient must be medically treated in preparation for surgery. Surgery can only proceed when the likelihood of intraoperative hypertension is reduced, so the



medical treatment of choice is phenoxybenzamine, a nonspecific and irreversible  $\alpha$ -blocker.

(A) Although giving a  $\beta$ -blocker in combination with an  $\alpha$ -blocker has been recommended by some scholars for rate control, a pure  $\beta$ -blocker such as atenolol should never be given as single therapy with a pheochromocytoma due to the unopposed  $\alpha$ -agonism that would result in severe hypertension. (C) Lisinopril is an ACE inhibitor often used in the treatment of hypertension (particularly diabetic patients for preventing the development of diabetic nephropathy), but not recommended as first-line medical treatment for pheochromocytoma. (D) Clonidine is a centrally acting  $\alpha$ -2 agonist used in the treatment of hypertension. Although not used as a diagnostic modality in current practice anymore, a clonidine suppression test served to help make the diagnosis of pheochromocytoma.

20

A 31-year-old woman presents with difficulty breastfeeding. She recently birthed a healthy baby boy via normal vaginal delivery with what she describes as “moderately heavy blood loss.” The patient also has noted diffusely dry skin, cold intolerance, and weight gain. She has not initiated her menstrual cycle yet. Physical examination reveals diffuse xerosis and thinning hair.

Which of the following is the likely diagnosis?

- (A) Autoimmune hypophysitis
- (B) Hashimoto thyroiditis
- (C) Premature ovarian failure
- (D) Sheehan syndrome

**The answer is D: Sheehan syndrome.** The patient in this question is presenting with postpartum pituitary gland necrosis, also known as Sheehan syndrome. The cause of this disease is ischemic necrosis due to blood loss (sometimes hypovolemic shock) during and after childbirth. Sheehan syndrome can be explained first by the enlargement of the anterior pituitary gland (hypertrophy of lactotrophs) during pregnancy without an increase in vascular supply. Therefore, if childbirth is accompanied by hemorrhage or hypotension, the pituitary gland is vulnerable to necrosis. Of note, the posterior pituitary gland is not affected because it is directly supplied by arterial blood (as opposed to the anterior pituitary that is supplied venously). The most common symptom of Sheehan syndrome is absence of lactation (agalactorrhea) or difficulty lactating. Women can also present with hypothyroidism (but usually years after the episode) and adrenal insufficiency. Deficient gonadotropin release will cause amenorrhea and growth hormone deficiency is difficult to assess clinically but is associated with fatigue and somewhat decreased muscle mass.

(A) Autoimmune hypophysitis is associated with lymphocytic infiltration of anterior pituitary cells and usually takes well over 10 years for autoimmune

symptoms to result. The symptoms are similar to Sheehan syndrome and include adrenal insufficiency, hypothyroidism, and hypogonadism; however, as opposed to agalactorrhea as seen in Sheehan syndrome, autoimmune hypophysitis can cause interruption of dopamine into the pituitary gland, which will cause an elevated prolactin level and cause milk production. (B) Hashimoto thyroiditis is an autoimmune disease of the thyroid gland, characterized pathologically by diffuse lymphocytic infiltration. Several antibodies are associated with Hashimoto thyroiditis, including thyroid peroxidase (TPO) antibodies and thyroglobulin antibodies. Given that this patient had not only presented with hypothyroid symptoms but also agalactorrhea, Hashimoto is unlikely. (C) Premature ovarian failure (POF) is an etiology of hypergonadotropic hypogonadism. The age of onset varies widely, but is defined as the loss of functional ovaries by the age of 40. It is associated with high levels of follicle-stimulating hormone (FSH) and decreased estrogen levels. Given this patient's recent vaginal delivery in addition to her hypothyroid symptoms, POF is highly unlikely to be the diagnosis.

**21** A 67-year-old woman with a history of GERD and congestive heart failure presents for her annual physical examination. Even though she has had no fractures, you recommend a DEXA scan to screen for osteoporosis.

What is the standard deviation threshold for beginning bisphosphonate therapy to treat osteoporosis?

- (A) T-score  $<-1$
- (B) T-score  $<-1.5$
- (C) T-score  $<-2.5$
- (D) T-score  $<-3$
- (E) T-score  $<-3.5$

**The answer is C: T-score  $<-2.5$ .** Treatment with bisphosphonates (such as alendronate) is typically started if the T-score is  $-2.5$  standard deviations below the mean. T-score is defined as the bone mineral density (BMD) at the site when compared to the *young normal reference mean* (healthy 30-year-old). This is in contrast to Z-score, which compares to the *age-matched normal*. If the T-score is between  $-1$  and  $-2.5$ , the diagnosis is osteopenia. If the T-score is below  $-2.5$ , then osteoporosis is diagnosed and a bisphosphonate should be started. Z-scores are typically used only when severe osteoporosis is suspected. Z-scores are also used in premenopausal women and in children.

**22** A 42-year-old female nurse presents with confusion, dizziness, shakiness, and insatiable hunger. She denies any past medical history and reports that these symptoms have persisted for the last 2 months. Orange juice makes her feel better. She has a temperature of  $37.2^{\circ}\text{C}$ ,

blood pressure of 120/78 mmHg, heart rate of 92 beats per minute, respiratory rate of 14 breaths per minute, and oxygen saturation of 98% on room air. Laboratory results reveal the following.

|                          |                                        |
|--------------------------|----------------------------------------|
| Glucose                  | 32 mg/dL                               |
| C-peptide                | 10.2 ng/mL (normal range, 0.5–3 ng/mL) |
| Insulin                  | Elevated                               |
| Urine sulfonylurea level | Undetectable                           |

Which of the following is the most likely diagnosis?

- (A) Factitious hypoglycemia from surreptitious injection of insulin
- (B) Insulinoma
- (C) Somatization disorder
- (D) Glucagonoma

**The answer is B: Insulinoma.** The patient in this question is presenting with clinical symptoms and laboratory findings consistent with an insulinoma, a pancreatic  $\beta$ -cell tumor that secretes excessive insulin. (A) This question presents a nurse, which many students automatically associate with surreptitious injection of insulin in a hypoglycemic patient. However, this patient presents with an elevated C-peptide level, which is consistent with an *endogenous* source of insulin since pancreatic  $\beta$ -cells produce proinsulin (which breaks down into insulin and C-peptide). Therefore, insulinoma is likely the diagnosis since there are increased levels of both insulin and C-peptide in this patient. Note that surreptitious sulfonylurea use will also produce elevated insulin and C-peptide levels since this drug essentially stimulates proinsulin secretion. That is why it is critical to order a urine sulfonylurea level, which is undetectable in this patient. (C, D) Somatization disorder and glucagonoma do not produce hypoglycemia.

23

A 28-year-old man presents with severe watery diarrhea for the past 6 months. He also endorses “feeling flushed” and several episodes of wheezing. He has an insignificant past medical history. Vital signs are within normal limits and the patient is afebrile. Physical examination reveals a 3/6 holosystolic murmur at the left lower sternal border.

What is the next best step in management of this patient?

- (A) Stool culture
- (B) Colonoscopy
- (C) Plasma catecholamine level
- (D) Urine 5-hydroxyindoleacetic acid (5-HIAA) level

**The answer is D: Urine 5-hydroxyindoleacetic acid (5-HIAA) level.**

The patient in this question is presenting with signs and symptoms of carcinoid syndrome. This is an uncommon syndrome caused by carcinoid tumors derived from neuroendocrine cells of the GI tract. The tumor secretes high levels of serotonin (5-HT). 5-HIAA is a breakdown product of 5-HT and thus will be elevated in this syndrome. Of note, symptoms of this syndrome (diarrhea, flushing, wheezing, and right-sided valvular disease) are not seen if the carcinoid tumor is limited to the GI tract (most commonly in the appendix). This is because 5-HT undergoes a first-pass metabolism in the liver. Carcinoid syndrome is also sometimes associated with niacin deficiency since tryptophan is used in the synthesis of niacin and in carcinoid syndrome there is increased tryptophan metabolism into serotonin. Niacin deficiency is associated with “the 3Ds”: depression, diarrhea, and dermatitis (pellagra). Treatment of carcinoid syndrome is with octreotide. (A, B) If this was a purely chronic diarrhea, stool culture might be warranted. However, supporting symptoms here establish carcinoid syndrome as the diagnosis. (C) Plasma catecholamine levels are increased in pheochromocytoma.

**24**

A 32-year-old man with no significant past medical history presents for follow-up of recently diagnosed hypertension. One month ago he fractured his tibia in a motorcycle accident and was found to have a blood pressure of 156/92 mmHg in the Emergency Department. Throughout his inpatient stay, his blood pressure remained elevated with systolic blood pressure readings consistently in the 150s. Workup was unremarkable and he was given low-dose hydrochlorothiazide to take once per day. Today his blood pressure is 148/88 mmHg and physical examination is unremarkable. Laboratory results reveal the following.

|                     |           |
|---------------------|-----------|
| Sodium              | 148 mEq/L |
| Potassium           | 2.6 mEq/L |
| Blood urea nitrogen | 16 mg/dL  |
| Creatinine          | 0.8 mg/dL |

What is the next best step in management of this patient?

- (A) Serum thiazide level
- (B) Plasma aldosterone concentration to plasma renin activity ratio
- (C) CT angiography of the abdomen
- (D) Plasma catecholamine level

**The answer is B: Plasma aldosterone concentration to plasma renin activity ratio.** This patient is quite young and healthy to have a diagnosis of hypertension and should raise suspicion for a secondary cause of hypertension. The patient has not improved significantly on hydrochlorothiazide and given the presence of hypokalemia in the setting of high blood pressure, he likely has primary hyperaldosteronism. The screening test of choice is early morning plasma aldosterone concentration (PAC) to plasma renin activity (PRA) ratio. In primary hyperaldosteronism, we expect aldosterone to be high and renin to be low (from the increased kidney perception of high intravascular volume), so the PAC/PRA ratio should be greater than 20.

(A) Thiazide diuretics can indeed cause hypokalemia, but this patient is taking a low dose once per day and his degree of hypokalemia cannot solely be due to a thiazide diuretic. Furthermore, this patient is slightly hypernatremic, which further lends credence to the diagnosis of primary hyperaldosteronism. (C) CT angiography of the abdomen is warranted in screening for secondary hypertension caused by renal artery stenosis or fibromuscular dysplasia. However, these are causes of *secondary* hyperaldosteronism and the PAC/PRA ratio will be less than 10 in these patients. Secondary hyperaldosteronism could indeed be the diagnosis, but the first step in management is still to obtain PAC and PRA levels before pursuing such a modality. (D) Plasma catecholamine levels are increased in pheochromocytoma.

25

A 51-year-old woman with a history of type 2 diabetes mellitus presents with nausea, vomiting, and bloating. She reports not being able to finish her meals like she used to since she “gets full easily.” She has needed insulin for diabetic control for the last 9 years. Her home monitor blood glucose readings have been in the high 200s and low 300s for the last 2 weeks. Physical examination is significant for an obese woman with decreased sensation to pinprick and soft touch bilaterally in her lower extremities.

Which of the following is a therapeutic option for this patient’s condition?

- (A) *Helicobacter pylori* triple therapy
- (B) Omeprazole
- (C) Erythromycin
- (D) Ranitidine

**The answer is C: Erythromycin.** The patient in this question has diabetic gastroparesis, otherwise known as delayed gastric emptying. This is caused by diabetic autonomic neuropathy of the gastrointestinal tract. This is a common condition in patients with longstanding diabetes and manifests as anorexia, nausea, vomiting, and early satiety. Treatment of diabetic gastroparesis is multifactorial and involves increasing dietary fiber, changing the

diet to include small, numerous meals, and using a prokinetic medication to help in gastric emptying. Both metoclopramide and erythromycin have prokinetic and antiemetic properties. Erythromycin is commonly used in an intravenous form for acute gastroparesis. (A) The patient is not presenting with symptoms suggestive of peptic ulcer disease and *H. pylori* triple therapy is not indicated without proper testing. (B, D) Omeprazole, a proton pump inhibitor, and ranitidine, a histamine H2 antagonist, are helpful as first-line treatments in the treatment of GERD, but are not useful in patients with gastroparesis.

26

A 33-year-old woman with a history of poorly controlled Graves disease is interested in radioactive iodine (RAI) therapy to permanently treat her hyperthyroidism. She is currently trying to get pregnant.

Which of the following should the physician warn the patient about as a possible side effect of RAI treatment?

- (A) Agranulocytosis
- (B) Recurrent laryngeal nerve injury
- (C) Worsening of Graves ophthalmopathy
- (D) First-trimester teratogenicity

**The answer is C: Worsening of Graves ophthalmopathy.** There are several ways to treat Graves disease. One option is antithyroid drugs such as propylthiouracil (PTU) and methimazole (MMI). If patients are interested in permanent treatment of their hyperthyroidism, then surgery (thyroidectomy) and RAI should be considered. With RAI treatment, iodine concentrates in the follicular cells of the thyroid and ablates them completely within 2 to 4 months. Although RAI therapy will treat the hyperthyroidism through destruction of thyroid tissue, it will not decrease circulating levels of TSH receptor antibodies, and thus it will not treat Graves ophthalmopathy. Through an unclear mechanism, it can actually worsen Graves ophthalmopathy. In order to prevent this, some practitioners give glucocorticoids prior to RAI treatment.

(A) Agranulocytosis is a side effect of antithyroid drugs (PTU and MMI). (B) Recurrent laryngeal nerve injury can occur in surgical thyroidectomy. (D) First-trimester teratogenicity can occur with MMI treatment. Therefore, a pregnant female interested in antithyroid medication should be offered PTU instead of MMI.

27

A 29-year-old woman presents with rapid hair growth over her torso and face for the last 2 months. During this time she has not menstruated; however, she reports always being “regular” in the past. Her boyfriend reports that she is looking more “masculine” than she did before and has developed acne and a lower voice. Her past medical history is

insignificant. On physical examination, a significant amount of coarse terminal hair is present on her jawline, chest, and lower abdomen. In addition, bitemporal hair thinning is noted. The patient refused genitourinary examination. Gynecologic ultrasound reveals normal and functionally intact ovaries.

Which of the following is the next best step in management?

- (A) 17-hydroxyprogesterone levels
- (B) Testosterone and DHEAS levels
- (C) LH and FSH levels
- (D) Abdominal CT scan

**The answer is B: Testosterone and DHEAS levels.** The patient in this question likely has an androgen-secreting neoplasm of either the ovary or the adrenal gland. She reports rapid onset of hyperandrogenism and virilization (acne, voice lowering, androgenic alopecia, and masculine features). Anytime a virilizing neoplasm is suspected, the first step is always to order serum testosterone and DHEAS levels. This will determine the likely site of the neoplasm: Increased testosterone levels with normal DHEAS levels make an androgen-secreting *ovarian* tumor likely, whereas increased DHEAS levels with normal or slightly increased testosterone levels make an androgen-secreting *adrenal* tumor likely. Of note, DHEAS (the sulfated form of DHEA) is exclusive to the adrenal glands; DHEA, on the other hand, is secreted from the ovaries and the adrenal glands. (A) 17-hydroxyprogesterone levels is the screening test in diagnosing congenital adrenal hyperplasia (CAH) and is elevated in the 21-hydroxylase and 11- $\beta$  hydroxylase deficiency forms of CAH. The classical form of this disease is usually diagnosed early in life and rapidly developing virilization is rare in this condition. (C) LH and FSH levels would be the answer if polycystic ovarian syndrome (PCOS) were suspected. PCOS, however, is very unlikely to have *rapidly* developing virilization. In PCOS, we typically see an increased ratio of LH to FSH. However, our patient is likely to have undetectable LH and FSH levels due to suppression by increased androgen levels. The lack of polycystic ovaries on ultrasound makes the diagnosis of PCOS unlikely with this patient. (D) Abdominal CT scan and other imaging studies are usually performed after serologic testing.

28

A 54-year-old woman presents with nausea and generalized muscle weakness. She was recently diagnosed with small cell lung cancer. She presents with a temperature of 36.8°C, blood pressure of 134/86 mmHg, heart rate of 96 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 96% on room air. Physical examination is unremarkable and laboratory results reveal the following.

|                     |                |
|---------------------|----------------|
| Sodium              | 126 mEq/L      |
| Potassium           | 3.7 mEq/L      |
| Chloride            | 95 mEq/L       |
| Bicarbonate         | 25 mEq/L       |
| Blood urea nitrogen | 11 mg/dL       |
| Creatinine          | 0.9 mg/dL      |
| Serum osmolality    | 238 mOsm/kg    |
| Urine osmolality    | 484 mOsm/kg    |
| Urine sodium        | 42 mEq/L       |
| TSH                 | 3.8 $\mu$ U/mL |

Which of the following do you expect to be present in this patient?

- (A) Peripheral edema
- (B) Paroxysmal nocturnal dyspnea
- (C) Delayed capillary refill time
- (D) No jugular venous distention

**The answer is D: No jugular venous distention.** The patient in this question has hyponatremia secondary to SIADH likely from small cell lung cancer. The key to answering this question is to recognize that SIADH causes *euvolemic* hyponatremia in which there is no volume expansion in the body, as opposed to hypovolemic hyponatremia (adrenal insufficiency, diuretic use) or hypervolemic hyponatremia (cirrhosis, congestive heart failure, nephrotic syndrome). Thus, physical examination will not demonstrate jugular venous distention. (A, B) Peripheral edema and paroxysmal nocturnal dyspnea are signs of hypervolemia. (C) Delayed capillary refill time is seen in hypovolemia.



- 29 A 54-year-old obese woman with a history of type 2 diabetes mellitus presents to the physician for her annual visit. She currently takes metformin and a multivitamin. She reports being compliant with her medication; however, she has noticed that her blood sugar levels have consistently been in the high 200s to 300s for the last month. Laboratory results reveal a fasting blood glucose of 172 mg/dL and an HbA1c of 8.3%. The physician informs her that a second agent will need to be prescribed for her diabetes. The patient requests an antidiabetic medication that will help her lose weight as well as control her blood sugars.



Which of the following medications should be added to the patient's current regimen?

- (A) Glipizide
- (B) Exenatide
- (C) Insulin
- (D) Pioglitazone

**The answer is B: Exenatide.** The preferred initial medication in patients with type 2 diabetes is metformin. Contraindications to metformin include renal insufficiency. Of note, metformin can cause adverse effects such as gastrointestinal irritation (diarrhea, cramps, increased flatulence) and lactic acidosis. However, most people with type 2 diabetes eventually require more than one medication for maintaining optimal glycemic control. If metformin is not sufficient in controlling a patient's blood sugars, then the second medication depends on several factors, one of which is patient preference. The patient here desires to lose weight as well as control her blood sugars, so a GLP-1 receptor agonist such as exenatide is used. (A) Although sulfonylureas (glipizide) are usually the second drug added to metformin in patients with suboptimal blood sugar levels, side effects include weight gain and hypoglycemia. (C) Insulin would definitely assist in improving glycemic control but is associated with weight gain and hypoglycemia. Insulin is usually added to metformin if HbA1c >8.5%. (D) A thiazolidinedione such as pioglitazone can be used in patients with renal insufficiency; however, it is associated with weight gain, CHF, and edema.



A 44-year-old woman with a history of type 2 diabetes presents with nausea, confusion, and lethargy. She has a temperature of 36.8°C, blood pressure of 134/86 mmHg, heart rate of 88 beats per minute, respiratory rate of 24 breaths per minute, and oxygen saturation of 94% on room air. Laboratory results reveal the following.

|                     |           |
|---------------------|-----------|
| pH                  | 7.3       |
| PaO <sub>2</sub>    | 94 mmHg   |
| PaCO <sub>2</sub>   | 30 mmHg   |
| Sodium              | 136 mEq/L |
| Potassium           | 3.7 mEq/L |
| Chloride            | 110 mEq/L |
| Bicarbonate         | 16 mEq/L  |
| Blood urea nitrogen | 11 mg/dL  |
| Creatinine          | 0.9 mg/dL |

Which of the following is a possible cause of this acid–base abnormality?

- (A) Diarrhea
- (B) Diabetic ketoacidosis
- (C) Myasthenia gravis
- (D) High altitude
- (E) Vomiting

**The answer is A: Diarrhea.** The patient in this question is presenting with a nonanion gap metabolic acidosis. Given that the pH is less than 7.4, it is an acidosis. To determine if it is a metabolic acidosis versus respiratory acidosis, one must then look at the  $\text{PaCO}_2$  and bicarbonate. If bicarbonate and  $\text{PaCO}_2$  are both low, it signifies that it is a metabolic acidosis since a decreased bicarbonate will signal the lungs to *hyperventilate* in order to decrease the  $\text{PaCO}_2$  to compensate for the decreased bicarbonate. Finally, the presence of an anion gap or nonanion gap must be determined. Anion gap (AG) represents the concentration of unmeasured serum anions and is calculated by subtracting the bicarbonate ( $\text{HCO}_3^-$ ) and the chloride (Cl) from the sodium [ $\text{AG} = \text{Na} - (\text{HCO}_3 + \text{Cl})$ ]. Normal anion gap value is between 6 and 12 mEq/L. This patient has an anion gap of 10, making this a nonanion gap metabolic acidosis. The most common cause of nonanion gap metabolic acidosis is diarrhea, which involves a GI loss of bicarbonate. (B) Diabetic ketoacidosis causes an anion gap metabolic acidosis. (C) Acute respiratory acidosis, on the other hand, occurs when inadequate ventilation occurs (so  $\text{CO}_2$  is retained (increased), which lowers the pH). This will then cause a rise in bicarbonate to compensate for the acidic pH. Myasthenia gravis and other neuromuscular diseases (muscular dystrophy, Guillain–Barré syndrome) are causes of respiratory acidosis. (D) High altitude causes a respiratory alkalosis since low atmospheric pressure of oxygen stimulates increased ventilation. (E) Vomiting causes a metabolic alkalosis.

**31** A 52-year-old woman presents with confusion and weakness for the last 2 weeks. Her husband reports that she has had three seizures during this time. She has an insignificant past medical history and her physical examination is unremarkable. Laboratory results reveal the following.

|                     |           |
|---------------------|-----------|
| Sodium              | 119 mEq/L |
| Potassium           | 4.0 mEq/L |
| Chloride            | 88 mEq/L  |
| Bicarbonate         | 22 mEq/L  |
| Blood urea nitrogen | 11 mg/dL  |
| Creatinine          | 0.9 mg/dL |

Rapid correction of this patient's electrolyte abnormality can cause which of the following?

- (A) Atrial fibrillation
- (B) Cerebral edema
- (C) Central pontine myelinolysis
- (D) Subarachnoid hemorrhage

**The answer is C: Central pontine myelinolysis.** The patient in this question has severely symptomatic hyponatremia (serum sodium  $<120$  mEq/L). This is a medical emergency and prompt correction of the serum sodium concentration with hypertonic (3%) saline should be initiated, while working up the underlying etiology. The maximum rate of serum sodium correction should be 0.5 mEq/L/h; if the rate is corrected too rapidly, then irreversible brain damage can occur from a condition called central pontine myelinolysis. This occurs because such rapid correction of hyponatremia can result in water moving from the intracellular compartment to the extracellular compartment and such altered metabolic activity results in cell damage to the neurons and glia. (A, D) Atrial fibrillation and subarachnoid hemorrhage are not adverse effects of rapid correction of severe hyponatremia. (B) Intracerebral edema can happen when the opposite clinical scenario (rapidly correcting hypernatremia) occurs. This is due to water flowing into brain cells, which causes them to swell.

32

A 62-year-old man with a longstanding history of chronic obstructive pulmonary disease (COPD) presents for follow-up. The patient is on several medications, including albuterol and ipratropium. He is compliant with his medications, but often gets short of breath with minimal exercise.

Which of the following physiologic changes do you expect in this patient?

- (A) Hypoventilation and increased renal bicarbonate reabsorption
- (B) Hypoventilation and increased renal bicarbonate excretion
- (C) Hyperventilation and increased renal bicarbonate reabsorption
- (D) Hyperventilation and increased renal bicarbonate excretion

**The answer is A: Hypoventilation and increased renal bicarbonate reabsorption.** This patient likely has a chronic respiratory acidosis secondary to chronic lung disease (COPD). Hypoventilation occurs in COPD due to decreased responsiveness to hypoxia and hypercapnia as well as increased dead space ventilation. This hypoventilation causes retention of  $\text{PaCO}_2$  ( $\text{PaCO}_2 >40$  mmHg). The increase in  $\text{PaCO}_2$  causes a decrease in pH, and the kidney compensates by increasing bicarbonate reabsorption to counteract the decrease in pH in an attempt to bring it back to normal (7.4). (B, C, D) These are not the findings in chronic respiratory acidosis.

33

A 42-year-old woman presents with headache, rigors, weakness, weight loss, nausea, vomiting, abdominal pain, and new-onset “craving of salty foods.” She is febrile with a temperature of 39.8°C and has a blood pressure of 82/48 mmHg, heart rate of 102 beats per minute, respiratory rate of 24 breaths per minute, and oxygen saturation of 94% on room air. Physical examination reveals dry mucous membranes and diffuse muscle tenderness on palpation. She has cyanosis on her distal extremities and a generalized maculopapular rash with several areas of purpura. Laboratory results reveal the following.

|             |           |
|-------------|-----------|
| Sodium      | 122 mEq/L |
| Potassium   | 5.8 mEq/L |
| Chloride    | 100 mEq/L |
| Bicarbonate | 24 mEq/L  |

Serum cortisol is lower than expected after ACTH stimulation test.

Which of the following is the most likely diagnosis?

- (A) SIADH
- (B) Withdrawal of exogenous steroids
- (C) Waterhouse–Friderichsen syndrome (WFS)
- (D) Cushing syndrome

**The answer is C: Waterhouse–Friderichsen syndrome (WFS).** The patient in this question is presenting with signs and symptoms of adrenal crisis, likely from primary adrenal insufficiency caused by hemorrhagic infarction of the adrenal glands by *Neisseria meningitidis*, which is called WFS. This bacterial infection can cause massive hemorrhage into one or both of the adrenal glands leading to organ failure, hypotension, and rapidly developing adrenal insufficiency. Given that the ACTH stimulation test did not produce an increase in serum cortisol (as one would expect with normally functioning adrenal glands) in addition to the laboratory findings of hyponatremia and hyperkalemia, primary adrenal insufficiency is the likely diagnosis. The presence of severe sepsis in this patient makes the diagnosis of WFS the most likely.

(A) SIADH would present with hyponatremia, but not hyperkalemia. (B) Withdrawal of exogenous steroids causes a *secondary* adrenal insufficiency. This would not present with fever and severe sepsis as in this patient. Furthermore, serum cortisol can sometimes increase (even if just a minimal amount) after ACTH stimulation in secondary adrenal insufficiency assuming there is still functional adrenal tissue. (D) Cushing syndrome presents with hypercortisolism, not hyponatremia.

34

A 29-year-old woman presents with complaints of weight loss, diarrhea, and sweating for the last 6 weeks. She is otherwise healthy and her family history is unremarkable. She has a temperature of 36.8°C, blood pressure of 142/86 mmHg, heart rate of 92 beats per minute, respiratory rate of 24 breaths per minute, and oxygen saturation of 98% on room air. Physical examination reveals moist warm skin and hyperreflexia.

Which of the following is the next best step in management?

- (A) Free T4 levels
- (B) Thyroid-stimulating hormone (TSH) levels
- (C) Thyroglobulin levels
- (D) Radioactive iodine uptake (RAIU) scan

**The answer is B: Thyroid-stimulating hormone (TSH) levels.** The patient in this question is demonstrating clinical manifestations of hyperthyroidism. In approaching the diagnosis of thyroid disorders, the first step is to order a TSH level. TSH is the *most sensitive* test to detect primary hypothyroidism and hyperthyroidism. Based on the TSH level, additional tests can be performed. (A) Free T4 is important in the diagnostic workup of thyroid disorders and should be the next test ordered if TSH comes back decreased. If free T4 is increased with a decreased TSH level, this is diagnostic of primary hyperthyroidism. If free T4 is decreased with a decreased TSH level, then central hypothyroidism is the diagnosis and the etiology involves the pituitary gland or the hypothalamus. Finally, if free T4 is normal with a decreased TSH, then this is subclinical hypothyroidism. (C) Thyroglobulin is often increased in goiter and hyperthyroidism and is also a tumor marker for thyroid cancer. It is not the best first test in working up thyroid disorders. (D) Radioactive iodine uptake (RAIU) scan is the next best step once primary hyperthyroidism is diagnosed (increased free T4 with decreased TSH) as it can help differentiate causes of hyperthyroidism (Graves vs. multinodular goiter vs. silent thyroiditis).

35

A 54-year-old woman with a history of type 1 diabetes mellitus and autoimmune thyroid disease presents with weakness, easy fatigability, anorexia, nausea, and vomiting. She has a blood pressure of 82/64 mmHg and physical examination reveals “spotty” hyperpigmentation of her mucous membranes in her oral cavity. Laboratory results reveal a potassium of 6.1 mEq/L and an elevated ACTH level.

Which of the following is the underlying diagnosis in this patient?

- (A) MEN type 1
- (B) MEN type 2A
- (C) Polyglandular autoimmune syndrome type I
- (D) Polyglandular autoimmune syndrome type II

**The answer is D: Polyglandular autoimmune syndrome type II.** The patient in this question is presenting with signs, symptoms, and laboratory findings consistent with primary adrenal insufficiency (adrenal dysfunction, hyperkalemia, and hypotension). We know this is *primary* adrenal insufficiency because ACTH is elevated as there is no negative feedback on the hypothalamic-pituitary axis since the adrenals are not functioning and secreting cortisol. *Secondary* adrenal insufficiency, on the other hand, is associated with low to normal levels of ACTH. Given that this patient has type 1 diabetes and autoimmune thyroid disease as well, this is diagnostic of polyglandular autoimmune syndrome type II. (C) Polyglandular autoimmune syndrome type I is usually found in children and is associated with mucocutaneous candidiasis, hypoparathyroidism, and adrenal insufficiency. (A) MEN type I is associated with parathyroid hyperplasia, pancreatic neoplasia, and pituitary adenoma. (B) MEN type 2A is associated with medullary thyroid carcinoma, pheochromocytoma, and parathyroid hyperplasia.

**36** A 42-year-old woman presents with sweating and palpitations. She has a blood pressure of 140/90 mmHg and her pulse is 78 beats per minute. Physical examination reveals a 3.5-cm nonmobile, hard, nontender thyroid nodule. The physician decides to perform a RAIU scan.

Which of the following features is not associated with an increased risk of malignancy?

- (A) Hard and immobile mass
- (B) Cold nodule on RAIU
- (C) Cervical lymphadenopathy
- (D) Hot nodule on RAIU

**The answer is D: Hot nodule on RAIU.** Thyroid nodules are fairly common with a 5% to 10% prevalence. Approximately 5% of thyroid nodules are malignant. (A, B, C) Factors associated with malignancy include history of radiation to the neck, male sex, hard and immobile mass, age greater than 70 years, worrisome ultrasound findings such as irregular borders and microcalcifications, cervical lymphadenopathy, and cold nodule on RAIU. Cold nodules are nonfunctional and do not absorb the radioiodine. Hot nodules, on the other hand, are autonomous (toxic) and readily absorb the radioiodine. However, hot nodules are benign and not associated with malignancy.

**37** A 53-year-old man presents with diffuse joint pain, headache, macroglossia, and reports that his jaw looks larger now than it did in previous photos. Physical examination reveals acanthosis nigricans and numerous skin tags in the axillary and groin regions. The patient has an enlarged jaw and is noted to have a hoarse voice.

Which of the following is the next best step in management?

- (A) Growth hormone (GH) level
- (B) Insulin-like growth factor 1 (IGF-1) level
- (C) Pituitary MRI
- (D) Colonoscopy

**The answer is B: Insulin-like growth factor 1 (IGF-1) level.** The patient in this question likely has acromegaly, a pituitary abnormality in which there is increased secretion of GH. GH circulates and stimulates production of IGF-1, an endocrine hormone produced primarily by the liver. In acromegaly, IGF-1 level is the best initial diagnostic study to perform. (A) GH levels fluctuate due to pulsatile secretion, so there is no utility in ordering GH levels for diagnostic purposes. However, some practitioners use an oral glucose tolerance test in which GH is not suppressed to  $<1$  ng/mL by 2 hours. (C) Pituitary MRI would be the next best step after confirming the diagnosis of acromegaly with an increased IGF-1 in order to evaluate for the presence of a tumor. (D) Colonoscopy has no diagnostic merit in acromegaly. However, patients with acromegaly are at risk for colonic polyps and an increased risk for colon cancer.

38

A 62-year-old man with a history of congestive heart failure (CHF) presents with confusion, nausea, and vomiting. Physical examination reveals peripheral edema, bibasilar crackles, and jugular venous distention. The patient is found to have a sodium level of 112 mEq/L. The physician places the patient on free water restriction.

Which of the following laboratory values do you expect with respect to the fractional excretion of sodium (FENa) and urine sodium (UNa) with this condition?

- |     | FENa   | UNa         |
|-----|--------|-------------|
| (A) | $>1\%$ | $<10$ mEq/L |
| (B) | $>1\%$ | $>20$ mEq/L |
| (C) | $<1\%$ | $<10$ mEq/L |
| (D) | $<1\%$ | $>20$ mEq/L |

**The answer is C: FENa  $<1\%$  and UNa  $<10$  mEq/L.** The patient in this question is hypervolemic (peripheral edema, bibasilar crackles, and jugular venous distention). Furthermore, he is severely hyponatremic (Na 112 mEq/L). The differential of hypervolemic hyponatremia includes CHF, cirrhosis, nephrotic syndrome, and advanced renal failure. The patient's hypervolemic hyponatremia is likely secondary to his underlying CHF. Given that in CHF there is decreased effective arterial volume (EAV) from the decreased cardiac output, the kidneys compensate by absorbing more sodium. Thus, we expect urine sodium (UNa) to be low ( $<10$  mEq/L) because it is mostly absorbed into the blood in response to diminished EAV. With similar reasoning, FENa will

be low as well ( $<1\%$ ). (B) In advanced renal failure, there is decreased kidney function and thus sodium is not able to be reabsorbed;  $\text{FENa}$  and  $\text{UNa}$  will be higher than normal ( $>1\%$  and  $>20 \text{ mEq/L}$ , respectively) since sodium is predominantly being excreted.



A 24-year-old woman presents with labored breathing and abdominal pain. She endorses polydipsia and polyuria. She has a blood pressure of 130/90 mmHg, her pulse is 120 beats per minute, and her respiratory rate is 24 breaths per minute. Laboratory results reveal the following.

|             |           |
|-------------|-----------|
| Sodium      | 134 mEq/L |
| Potassium   | 3.9 mEq/L |
| Chloride    | 94 mEq/L  |
| Bicarbonate | 16 mEq/L  |
| Creatinine  | 1.0 mg/dL |
| Glucose     | 880 mg/dL |

She is treated with intravenous insulin and isotonic saline solution. Two hours later her serum glucose concentration is 410 mg/dL with ample urine output.

Which of the following is the most appropriate next step?

- (A) Add glucose to the IV solution
- (B) Add potassium to the IV solution
- (C) Initiate treatment with intermediate-acting insulin
- (D) Discontinue isotonic saline solution and begin hypotonic saline solution

**The answer is B: Add potassium to the IV solution.** The patient in this question is presenting in DKA. DKA is characterized by an elevated glucose (400 to 800 mg/dL) in the setting of abdominal pain, nausea/vomiting, Kussmaul respirations, “fruity” breath, dehydration, polydipsia, polyuria, polyphagia, and altered mental status. Since this causes an anion gap metabolic acidosis, patients often present with hypokalemia as well. The treatment is heavy IV fluids and IV insulin. Since insulin causes an intracellular shift of potassium, potassium should be added to the replacement solution (10 to 20 mEq/L) once urine output is ample and the serum potassium is  $<6.0 \text{ mEq/L}$ . (A) Glucose should only be added once blood glucose reaches 250 mg/dL. (C) Intermediate-acting insulin can be given instead of continuous IV insulin



once the anion gap has been corrected and the patient can tolerate PO intake. (D) Hypotonic saline solution has no role in the treatment of DKA.



A 29-year-old woman presents for follow-up after a fine-needle aspiration biopsy of a thyroid nodule showed malignant cells.

Which of the following types of thyroid cancer is the most common?

- (A) Follicular
- (B) Papillary
- (C) Medullary
- (D) Anaplastic

**The answer is B: Papillary.** Papillary thyroid cancer is the most common type, and fortunately the least aggressive. It spreads via lymphatics and is histopathologically characterized by nuclear grooves, pseudoinclusions, and psammoma bodies. Papillary thyroid cancer has an excellent prognosis when compared to the other types. (A) Follicular thyroid cancer is known for its vascular/capsular invasion and hematogenous spread. Prognosis is fair. (C) Medullary thyroid cancer is seen in the MEN II syndromes and arises from parafollicular (C) cells. Calcitonin is the tumor marker and the cancer spreads via lymphatics. Medullary thyroid cancer is histopathologically characterized by amyloid and has a fair prognosis. (D) Anaplastic thyroid cancer has the poorest prognosis of the different types of thyroid cancer, is exceedingly rare/malignant, and histopathologically is undifferentiated without any resemblance to thyroid tissue.



## Infectious Diseases

1

A 72-year-old woman is admitted to the hospital for an acute exacerbation of heart failure. She has a history of congestive heart failure (CHF), hypertension, and diabetes. While in the hospital, she is diuresed with IV furosemide and her symptoms improve. However, 3 days later she develops worsening shortness of breath. Her temperature is 38.1°C, blood pressure is 104/68 mmHg, heart rate is 94 beats per minute, respiratory rate is 26 breaths per minute, and oxygen saturation is 92% on room air. A chest x-ray is ordered and is shown in *Figure 6-1*.



**Figure 6-1**

What is the most appropriate empiric treatment?

- (A) Ceftriaxone and azithromycin
- (B) Ceftriaxone, levofloxacin, and vancomycin
- (C) Clindamycin
- (D) Increase the dose of IV furosemide and administer morphine

**The answer is B: Ceftriaxone, levofloxacin, and vancomycin.** In a patient with pneumonia, it is important to first define the type of pneumonia since this identifies the likely organism and the necessary empiric antibiotic therapy. Hospital-acquired pneumonia (HAP) refers to the development of pneumonia >48 hours after admission, with no evidence of pneumonia on admission. A type of HAP is ventilator-associated pneumonia (VAP), which occurs 48 to 72 hours after mechanical ventilation.

**Table 6-1 Common Etiologies of Pneumonia and Empiric Antibiotic Regimens**

| Most Common Organisms                                                                                                                                            | First-Line Empiric Antibiotics                                                                                                                                                                                                                                                                                                                                                                                          |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| CAP: <i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Mycoplasma</i> , many others                                                                               | <ul style="list-style-type: none"><li>• Outpatient: macrolide or doxycycline<br/>E.g., azithromycin</li><li>• Inpatient: (anti-pneumococcal <math>\beta</math>-lactam + macrolide) or fluoroquinolone<br/>E.g., ceftriaxone + clarithromycin</li><li>• ICU level: anti-pneumococcal <math>\beta</math>-lactam + (macrolide or fluoroquinolone) + vancomycin<br/>E.g., ceftriaxone + levofloxacin + vancomycin</li></ul> |
| VAP/HAP/HCAP: GNRs ( <i>Pseudomonas</i> , <i>Klebsiella</i> , <i>E. coli</i> , <i>Stenotrophomonas</i> ), <i>S. aureus</i> (MSSA and MRSA), <i>Acinetobacter</i> | <ul style="list-style-type: none"><li>• Without risk factors for MDR organisms: ampicillin-sulbactam or ceftriaxone or ertapenem or fluoroquinolone</li><li>• With risk factors for MDR organisms: anti-pseudomonal antibiotic + anti-MRSA + (fluoroquinolone or aminoglycoside)<br/>E.g., piperacillin-tazobactam + vancomycin + gentamicin</li></ul>                                                                  |
| Aspiration PNA: oropharyngeal microbes                                                                                                                           | No consensus; clindamycin or amoxicillin-clavulanate are good options; metronidazole should not be used as monotherapy                                                                                                                                                                                                                                                                                                  |

CAP, community-acquired pneumonia; VAP, ventilator-associated pneumonia; HAP, hospital-acquired pneumonia; HCAP, healthcare-associated pneumonia; GNR, gram-negative rod; MDR, multidrug resistant; PNA, pneumonia.

Healthcare-associated pneumonia (HCAP) develops in a patient with recent or ongoing contact with healthcare facilities or personnel (e.g., hospitalized  $\geq 2$  days in the last 90 days, lives in a long-term care facility, receives dialysis, etc.). Finally, community-acquired pneumonia (CAP) refers to pneumonia that develops in all other patients. *Table 6-1* shows the common organisms causing each type of pneumonia as well as the appropriate empiric antibiotic therapy.

(A) Empiric antibiotics for inpatient CAP consist of an anti-pneumococcal  $\beta$ -lactam (e.g., ampicillin-sulbactam, ceftriaxone, cefotaxime, ceftazidime, ertapenem) and a macrolide (e.g., azithromycin or clarithromycin). An alternative is a respiratory fluoroquinolone alone (e.g., levofloxacin, moxifloxacin). (C) Clindamycin is a good agent to use for suspected aspiration pneumonia and may be used as monotherapy. (D) This answer would be correct if the patient's heart failure symptoms were not improving; however, the presence of fever and consolidation on chest x-ray indicate pneumonia.



A 29-year-old woman presents to the hospital with fever, headache, and cough. She developed these symptoms 2 days ago, and now also endorses some shortness of breath. She denies any rash, neck stiffness, recent travel, or sick contacts, and she has received all of her immunizations including her annual influenza vaccine. She lives in Connecticut and has several dogs. She is febrile to  $38.7^{\circ}\text{C}$ , but the rest of her examination is unremarkable. Her laboratory values are shown below.

|                            |                      |
|----------------------------|----------------------|
| Hemoglobin                 | 11.0 g/dL            |
| Leukocyte count            | $2,700/\text{mm}^3$  |
| Platelets                  | $98,000/\text{mm}^3$ |
| Blood urea nitrogen        | 22 mg/dL             |
| Creatinine                 | 1.4 mg/dL            |
| Aspartate aminotransferase | 69 U/L               |
| Alanine aminotransferase   | 58 U/L               |
| Alkaline phosphatase       | 110 U/L              |
| Lactate dehydrogenase      | 160 U/L              |

Which of the following is the most likely causative organism?

- |                                     |                                   |
|-------------------------------------|-----------------------------------|
| (A) <i>Borrelia burgdorferi</i>     | (F) <i>Yersinia pestis</i>        |
| (B) <i>Ehrlichia chaffeensis</i>    | (G) <i>Babesia microti</i>        |
| (C) Influenza A/B                   | (H) <i>Rickettsia rickettsii</i>  |
| (D) <i>Francisella tularensis</i>   | (I) <i>Neisseria meningitidis</i> |
| (E) <i>Streptococcus pneumoniae</i> | (J) Parvovirus B19                |

**The answer is B: *Ehrlichia chaffeensis*.** Nonspecific flu-like symptoms associated with leukopenia, thrombocytopenia, transaminitis, anemia, and an elevated creatinine are strongly suggestive of ehrlichiosis/anaplasmosis. *Ehrlichia chaffeensis* is carried by the *Dermacentor variabilis* tick (which can also carry *Rickettsia rickettsii*) or the *Amblyomma americanum* tick and causes human monocytic ehrlichiosis; *Anaplasma phagocytophilum* is carried by the *Ixodes* tick (which may also carry *Borrelia burgdorferi* and *Babesia microti*, and coinfection can occur), and causes human granulocytic anaplasmosis. Both are gram-negative obligate intracellular bacteria that can produce the above clinical findings, and therefore they are often described together. The diagnosis is typically made with PCR, since the finding of intraleukocytic morulae on peripheral blood smear may be seen but is not a sensitive test. Treatment is with doxycycline.

Although many of the other answer choices can produce the nonspecific symptoms seen in this patient, the laboratory abnormalities point to the diagnosis of *E. chaffeensis*/*A. phagocytophilum* infection. (A, D, G, H) These answer choices are other important tick-borne illnesses. *B. burgdorferi* causes Lyme disease, which presents with the rash of erythema migrans. *F. tularensis* can occur through contact with ticks or animal tissues and will produce a necrotic eschar at the site of infection and lymphadenopathy. *B. microti* can cause a severe hemolytic anemia, and a peripheral blood smear shows the parasite within red blood cells (RBCs). *R. rickettsii* causes Rocky Mountain spotted fever, which presents with a rash that starts peripherally and spreads centrally. (C) This patient had her annual influenza vaccine (though not 100% protective), and influenza would not produce the laboratory abnormalities seen in this patient. (E) *S. pneumoniae* is the most common cause of CAP and meningitis. (F) *Yersinia pestis* is carried by fleas and causes bubonic, pneumonic, or septicemic plague. (I) *Neisseria meningitidis* is a cause of meningitis and sepsis; the incidence has decreased since the introduction of the meningococcal vaccine. (J) Parvovirus B19 produces erythema infectiosum (fifth disease with the classic “slapped cheek” rash) in children, but in adults can produce arthralgias, aplastic crisis in patients with chronic hemolytic disease, miscarriage in pregnant patients, and chronic pure RBC aplasia in immunocompromised patients.



A 42-year-old man is brought to the hospital by his wife due to headache and a change in mental status. His wife reports that the symptoms

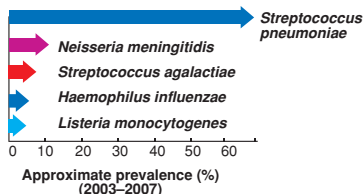
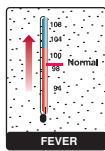
started yesterday and are getting worse. He has experienced migraines previously, but the pain and photophobia are much worse this time. He was not himself and was very confused this morning, so she brought him to the Emergency Department. His temperature is 38.8°C with a normal blood pressure and heart rate. There is moderate neck stiffness on examination with no focal neurologic deficits. A lumbar puncture is performed, and a Gram stain of the cerebrospinal fluid (CSF) shows gram-positive cocci.

What is the most likely pathogen, and what would be expected on CSF analysis? (Note: WBCs are white blood cells.)

|     | Organism                | WBCs   | Protein | Glucose |
|-----|-------------------------|--------|---------|---------|
| (A) | <i>S. aureus</i>        | ↑      | ↓       | ↓       |
| (B) | <i>S. pneumoniae</i>    | ↑      | ↑       | ↓       |
| (C) | <i>S. pneumoniae</i>    | ↑      | Normal  | Normal  |
| (D) | <i>S. pyogenes</i>      | Normal | ↑       | ↑       |
| (E) | <i>L. monocytogenes</i> | ↑      | Normal  | ↓       |
| (F) | <i>H. influenzae</i>    | ↑      | ↑       | ↓       |

**The answer is B: *S. pneumoniae*, ↑ WBCs, ↑ protein, ↓ glucose.** The Gram stain confirms that this patient has acute bacterial meningitis, which commonly presents with fever, headache, neck stiffness, and/or mental status changes. Other symptoms include photosensitivity and seizures. The most common causative organism is *S. pneumoniae*, which is a lancet-shaped diplococcus. Other common pathogens that cause meningitis are summarized in Figure 6-2.

The CSF findings in meningitis are high yield for the shelf examination. Bacterial meningitis will present with very elevated lymphocytes with a neutrophil predominance, low glucose, and elevated protein. Viral meningitis will present with elevated lymphocytes with a lymphocyte predominance (though there is often a neutrophil predominance early in the course of the infection), normal glucose, and mildly elevated protein. Fungal meningitis will have findings similar to viral meningitis, except that the glucose will be low. Meningitis due to tuberculosis (TB) will have findings similar to fungal meningitis, but other clues will be given to help make the diagnosis such as exposures, risk factors, and acid-fast bacilli (AFB) smear or culture.

**A Overview of common causes of bacterial meningitis in adults****C Common complaints****B Classification of pathogens****Gram (+) cocci**

*Streptococcus agalactiae*  
*Streptococcus pneumoniae*

**Gram (+) rods**

*Listeria monocytogenes*

**Gram (-) cocci**

*Neisseria meningitidis*

**Gram (-) rods**

*Haemophilus influenzae*

***Haemophilus influenzae***

- *H. influenzae* is a normal resident of the human upper respiratory tract. Transmission is by respiratory droplets.
- After attaching to and colonizing the respiratory mucosa, the infection can become systemic, with bacteria spreading via the blood to the CNS. *H. influenzae* was a leading cause of bacterial meningitis, especially in infants and young children. A conjugated vaccine against *H. influenzae* capsular polysaccharide type b is now administered to infants and has dramatically lowered the number of meningitis cases attributable to this organism.

***Listeria monocytogenes***

- *L. monocytogenes* infections are most common among older adults, pregnant women, fetuses or newborns, and immunocompromised individuals. Meningitis is a common presentation. Listeria infections, which may occur as sporadic cases or in small epidemics, are usually foodborne, with the organism entering the body via the GI tract.

***Neisseria meningitidis***

- *N. meningitidis* is a common cause of meningitis. Transmission is via respiratory droplets. Pili allow the attachment of *N. meningitidis* to the nasopharyngeal mucosa.
- If meningococci penetrate the epithelial lining of the nasopharynx and enter the bloodstream, they rapidly multiply, causing meningococemia. If *N. meningitidis* crosses the blood–brain barrier, it can infect the meninges, causing an acute inflammatory response that results in a purulent meningitis. The initial fever and malaise can rapidly evolve into severe headache, rigid neck, vomiting, and sensitivity to bright light. Coma can occur within a few hours. *N. meningitidis* is the most common cause of bacterial meningitis between the ages of 2 and 18 years.

***Streptococcus agalactiae***

- *S. agalactiae* causes meningitis and septicemia in neonates. It is found normally in the genital tract of female carriers and the urethral mucous membranes of male carriers, as well as in the gastrointestinal (GI) tract (especially the rectum). Transmission occurs during birth and is sexually transmitted among adults.
- Infection of an infant occurs as it traverses the birth canal. *S. agalactiae* infection is a leading cause of neonatal meningitis, and it has a high mortality rate.

***Streptococcus pneumoniae***

- *S. pneumoniae* is an important cause of meningitis and pneumonia. It is carried in the nasopharynx of many healthy individuals. Infection can be either endogenous (in a carrier who develops impaired resistance to the organism) or exogenous (by droplets from the airway of a carrier).
- *S. pneumoniae* infections can result in a bacteremia leading to infection of several sites in the human body, including the central nervous system (CNS). This meningitis has a high mortality rate, even when treated appropriately. *S. pneumoniae* is the most common cause of bacterial meningitis in adults.

Figure 6-2



4

A 26-year-old man presents to his primary care physician complaining of fatigue, headache, and a sore throat for the past week. There is also nausea and diarrhea, but no weight loss, productive cough, or difficulty breathing. He denies any past medical history, does not take any medications, and has no recent sick contacts. He is sexually active with men and women and uses condoms inconsistently; he drinks alcohol heavily on the weekends and admits to previous IV drug use. On examination, his temperature is 39°C and the rest of his vital signs are normal. He has nontender cervical and axillary lymphadenopathy, tonsillar exudates, and mild splenomegaly. There are also several painful, well-demarcated ulcers within his mouth and a mild maculopapular rash over his chest and arms. A rapid strep test and a monospot (heterophile antibody) test are negative; further screening for chlamydia, gonorrhea, syphilis, and HIV is negative.

What is the most likely diagnosis?

- (A) Hodgkin lymphoma
- (B) Acute retroviral syndrome
- (C) Infectious mononucleosis
- (D) Secondary syphilis

**The answer is B: Acute retroviral syndrome.** Acute HIV infection can present in a variety of ways, but typical symptoms of the “acute retroviral syndrome” include a mononucleosis-like syndrome with fever, lymphadenopathy, headache, myalgias/arthritis, sore throat, and a maculopapular rash. Another less sensitive but more specific finding is painful, well-demarcated mucocutaneous ulcerations. Additional clues to the diagnosis in this case are the patient’s high risk behaviors (unprotected sex, IV drug use) and negative test results for other conditions on the differential diagnosis (mononucleosis due to EBV, syphilis and other STIs, etc.). During the acute phase of HIV infection, there may be a negative screening test (ELISA may take weeks to become positive) with high viral RNA levels. Typically, the diagnosis of HIV is made with a highly sensitive screening test (e.g., ELISA) followed by a more specific confirmatory test (e.g., Western blot).

(A) The finding of diffuse nontender lymphadenopathy is more consistent with a systemic process such as a viral infection rather than Hodgkin lymphoma, which often presents with focal or asymmetric lymphadenopathy. (C) Though heterophile-negative mononucleosis due to CMV is a possibility, the findings of both maculopapular rash and mucocutaneous ulcerations make HIV more likely (both may occur in CMV infection but are less common manifestations, and GI ulcerations usually occur in the setting of immunosuppression). (D) Secondary syphilis is less likely to have mucocutaneous ulcerations and the screening test was negative. Although false negatives are possible with RPR and VDRL tests, the constellation of findings makes HIV infection much more likely than a false-negative syphilis test.

5

A 65-year-old man is brought into the Emergency Department by his daughter, who reports that he is fatigued and short of breath. Several days ago he developed a fever with a productive cough, which has now progressed to dyspnea at rest. On examination, the patient's temperature is 38.6°C, his blood pressure is 74/42 mmHg, his heart rate is 96 beats per minute, his respiratory rate is 24 breaths per minute, and his oxygen saturation is 94% on room air. He is lethargic, his neck veins are flat, and his extremities are warm and moist. There is dullness to percussion and decreased breath sounds over the right lung base. Serum blood work shows an elevated lactate.

What is the correct diagnosis?

- (A) Cardiogenic shock
- (B) Pulmonary embolism
- (C) Sepsis
- (D) Severe sepsis
- (E) Septic shock
- (F) Anaphylactic reaction

**The answer is D: Severe sepsis.** This patient has severe sepsis secondary to pneumonia. It is important to know the definitions related to the topic of sepsis. Systemic inflammatory response syndrome (SIRS) is defined by two or more of the following: (1) temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ ; (2) a heart rate  $>90$  beats per minute; (3) a respiratory rate  $>20$  breaths per minute or a  $\text{PaCO}_2 <32$  mmHg; and (4) a serum leukocyte count  $>12,000/\text{mm}^3$  or  $<4,000/\text{mm}^3$  or  $>10\%$  bands. (C) With a suspected source of infection, it is called sepsis. Severe sepsis is the definition for sepsis with end-organ dysfunction, signified by hypotension or hypoperfusion (e.g., oliguria, elevated serum lactate, elevated liver enzymes, etc.). Septic shock is severe sepsis that does not respond to adequate fluid resuscitation. This patient meets SIRS criteria with a suspected source of infection (pneumonia) and hypotension; (E) IV fluids have not been administered yet, so the definition of septic shock is not met.

Septic shock is one type of distributive shock, which is characterized by hypotension with flat neck veins and warm extremities (low systemic vascular resistance). (F) Anaphylaxis is another form of distributive shock, but is unlikely since there was no history of recent exposures mentioned in the vignette (e.g., bee sting, new medication, etc.). (A, B) Both cardiogenic shock and pulmonary embolism (a type of obstructive shock) are ruled out by flat neck veins (which indicate hypovolemic or distributive shock). Finally, hypovolemic shock would present with flat neck veins and *cool* extremities, since systemic vascular resistance increases in an attempt to maintain blood pressure.

6

A 79-year-old woman presents to the Emergency Department from a nursing home with severe diarrhea and dehydration. The symptoms started yesterday and are associated with fever and abdominal pain. She has had approximately 15 nonbloody, watery bowel movements since then and has been getting weaker. Upon further questioning of the nursing home staff, she had pneumonia 1 week ago and is finishing treatment. Her other medical problems include hypothyroidism, hypertension, and coronary artery disease. Her temperature is 39.8°C, blood pressure is 96/64 mmHg, heart rate is 92 beats per minute, and respiratory rate is 18 breaths per minute. Initial screening laboratory values show a leukocyte count of 22,300/mm<sup>3</sup>, a hemoglobin of 13.8 g/dL, and a platelet count of 480,000/mm<sup>3</sup>. Further diagnostic workup is pending.

What is the most appropriate next step in management?

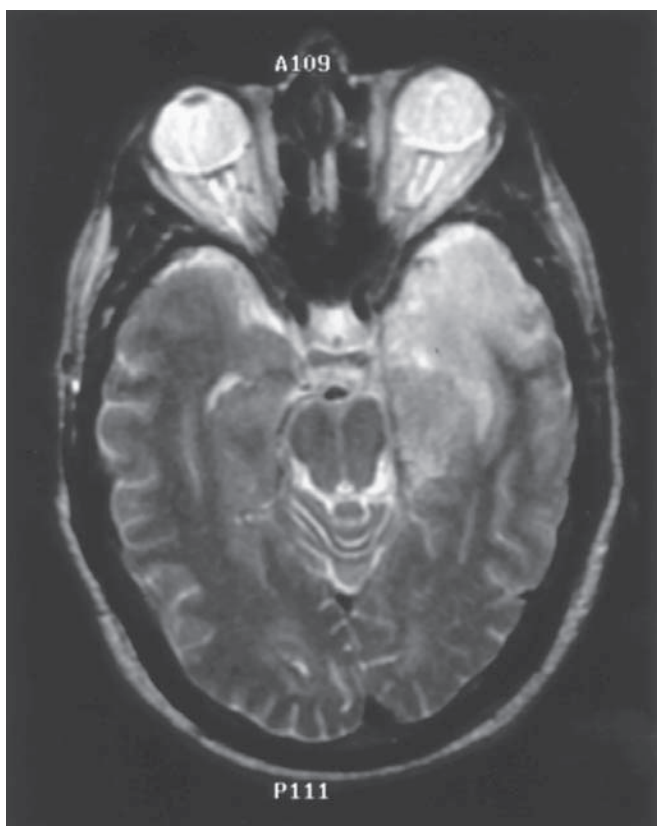
- (A) Decrease the patient's dose of levothyroxine
- (B) Immediate laparotomy
- (C) Oral metronidazole alone
- (D) IV vancomycin alone
- (E) Oral vancomycin and IV metronidazole

**The answer is E: Oral vancomycin and IV metronidazole.** This patient has a severe infection due to *Clostridium difficile*, which colonizes the intestinal tract and releases toxin A/B that damages the colonic mucosa. It is a very common nosocomial pathogen, and infection frequently occurs after antibiotics due to alteration of the gut flora. The severity can range from mild (loose stools without dehydration) to severe (profuse watery diarrhea, severe colitis, and toxic megacolon). Diagnosis can be made by testing the stool for *C. difficile* toxins, or with endoscopy showing pseudomembranous colitis. If *C. difficile* is suspected, the causative antibiotic should be stopped immediately and appropriate contact measures implemented (e.g., washing hands with soap and water upon entering and exiting the patient's room). In addition, antibiotics should be started, which are based on the severity of disease. Severe *C. difficile* infection (indicated by >12 bowel movements per day, high fever, serum leukocyte count >15,000/mm<sup>3</sup>, acute kidney injury, sepsis, age >65 or 70, etc.) should be treated with oral vancomycin since the drug has poor oral bioavailability, making it through the gut to act locally in the infected colon. Other options include oral vancomycin with IV metronidazole, or per rectal vancomycin with IV metronidazole (especially if the patient has an ileus). (C) Oral metronidazole alone is appropriate for mild infections; however, this patient is severely ill. (D) Oral vancomycin is preferred to IV vancomycin given its direct contact to infected colon.

(A) Iatrogenic hyperthyroidism can cause diarrhea, but would have other signs (marked tachycardia, mental status changes, etc.) without such a marked leukocytosis, as is seen in this patient. (B) Surgical colectomy is

an option for severe infections based on abdominal CT results (e.g., bowel perforation, toxic megacolon), but it is not the next step in management for this patient.

- 7** A 32-year-old man is brought into the Emergency Department after he had a seizure. He has no history of a seizure disorder and there was no preceding trauma, new medications, or illicit drugs. On examination, his temperature is 38.9°C, blood pressure is 118/70 mmHg, heart rate is 90 beats per minute, and respiratory rate is 12 breaths per minute. He is lethargic and has a horizontal gaze palsy affecting the left eye. Appropriate laboratory values are sent, and a lumbar puncture and MRI (*Figure 6-3*) are performed. The CSF studies show a large number of RBCs in each tube.



**Figure 6-3**

Which of the following therapies is most likely to be active against this condition?

- (A) Dexamethasone
- (B) Vancomycin
- (C) Amphotericin B
- (D) Acyclovir
- (E) Ceftriaxone

**The answer is D: Acyclovir.** The only medication on the list that has activity against herpes simplex virus type 1 (HSV-1) is acyclovir. HSV is the most common cause of sporadic encephalitis and has a very high morbidity and mortality. It presents acutely with fever, mental status changes, and focal neurologic deficits; affected patients may also have symptoms of meningitis. Whereas meningitis is caused by inflammation of the meninges surrounding the brain (infection of the subarachnoid space), encephalitis is caused by inflammation of the brain parenchyma. There is frequently overlap of the two conditions (meningoencephalitis).

Other findings in the above vignette that suggest this diagnosis are elevated RBCs in the CSF in each tube (as opposed to a traumatic spinal tap, in which the concentration of RBCs would diminish with each tube), and inflammation of the left temporal lobe seen on MRI. HSV should be highly suspected in any patient with encephalitis, and the above findings are virtually diagnostic of HSV; however, the diagnosis can be confirmed with PCR or viral culture of the CSF. If suspected, empiric acyclovir should be started immediately. One potential adverse reaction of acyclovir is acute renal failure, which can occur secondary to crystal formation in the tubules.

(A) Dexamethasone is a strong corticosteroid that can be used in cases of *S. pneumoniae* meningitis, which is not the likely diagnosis based on the MRI showing encephalitis. (B, E) Ceftriaxone and vancomycin are used for empiric antibiotic treatment of meningitis. Ceftriaxone is effective against *S. pneumoniae*, *N. meningitidis*, and *H. influenzae*, and vancomycin is effective against cephalosporin-resistant *S. pneumoniae* and *S. aureus*. (C) Amphotericin B is used for cryptococcal meningitis, which is the most common manifestation of *Cryptococcus neoformans* in HIV patients.



8 A 60-year-old man with a history of hypertension and chronic obstructive pulmonary disease (COPD) presents to the Emergency Department complaining of fever and a productive cough. The symptoms started yesterday and have been progressive. He now also has vomiting, diarrhea, headache, and muscle and joint pain. His current medications include inhaled albuterol and ipratropium, hydrochlorothiazide, and lisinopril. He has a 30 pack-year smoking history and drinks alcohol moderately. He recently returned from a business trip, where he stayed in several hotels and ate all of his meals within these hotels. On examination, his temperature

is 39.2°C with a heart rate of 110 beats per minute and a respiratory rate of 26 breaths per minute. Pulmonary examination reveals dullness to percussion in the left lower lobe with rales and bronchial breath sounds on auscultation. His laboratory values are shown below.

|                            |                         |
|----------------------------|-------------------------|
| Hemoglobin                 | 13.9 g/dL               |
| Leukocyte count            | 15,000/mm <sup>3</sup>  |
| Platelets                  | 130,000/mm <sup>3</sup> |
| Sodium                     | 128 mEq/L               |
| Potassium                  | 3.5 mEq/L               |
| Chloride                   | 95 mEq/L                |
| Bicarbonate                | 22 mEq/L                |
| Blood urea nitrogen        | 32 mg/dL                |
| Creatinine                 | 1.3 mg/dL               |
| Aspartate aminotransferase | 54 U/L                  |
| Alanine aminotransferase   | 62 U/L                  |
| Alkaline phosphatase       | 53 U/L                  |

A urine dipstick shows 1+ protein and 1+ blood.

Which of the following is the most likely causative organism?

- (A) *Streptococcus pneumoniae*
- (B) *Legionella pneumophila*
- (C) *Klebsiella pneumoniae*
- (D) *Pseudomonas aeruginosa*
- (E) *Mycoplasma pneumoniae*
- (F) *Haemophilus influenzae*
- (G) *Stenotrophomonas maltophilia*
- (H) *Peptostreptococcus anaerobius*

**The answer is B: *Legionella pneumophila*.** This patient has CAP with features of Legionnaires' disease caused by *L. pneumophila*, which is the most common *Legionella* species to cause disease in humans. It is a common cause of CAP and HAP. Although Legionnaires' disease can occur in any age group, it is more common in older patients who have a history of smoking or underlying

lung disease. This patient likely acquired this infection from recent travel; outbreaks typically involve a water source such as hotel drinking water. It presents as pneumonia with fever, productive cough, and dyspnea and may also have symptoms of headache, myalgias/arthralgias, nausea/vomiting, and diarrhea. Laboratory values frequently show hyponatremia, renal and/or hepatic dysfunction, and hematuria/proteinuria. Diagnosis can be made with a urinary antigen test and culture on buffered charcoal yeast extract agar. Treatment is with a macrolide or fluoroquinolone antibiotic. This is a high-yield question for the shelf examination; when an elderly patient presents with pneumonia, hyponatremia, and diarrhea, suspect *Legionella*. (Of note, *Legionella* can also cause a mild, self-limited pulmonary condition called Pontiac fever, though this is less common than Legionnaires' disease.)

Almost all of the answer choices are reasonable choices for CAP; however, the constellation of findings argues for *Legionella* over the other organisms. It is helpful to know the organisms associated with unique clinical syndromes (e.g., Legionnaires' disease) and with unique circumstances (e.g., *Nocardia* in an immunosuppressed patient). (A) *S. pneumoniae* is the most common cause of pneumonia worldwide. (C) *Klebsiella* is common in alcoholics and nursing home patients; look for the buzzwords "currant jelly sputum" and "muroid colonies." (D) *Pseudomonas* is a common water-loving nosocomial pathogen that is often multidrug resistant (MDR). It is also very common in cystic fibrosis patients. (E) *Mycoplasma* and other "atypical" pneumonias are common in young, healthy patients. (F) *H. influenzae* and *Moraxella catarrhalis* are common causes of pneumonia in COPD patients; however, the constellation of findings in this patient argues for *Legionella* over *H. influenzae*. (G) *Stenotrophomonas maltophilia* is an opportunistic MDR organism that can cause HAP and VAP. (H) *Peptostreptococcus anaerobius* is an anaerobic organism that is often found in cases of aspiration pneumonia.



A 46-year-old HIV-positive man is doing poorly on his antiretroviral regimen. He undergoes HIV genotyping and begins a new treatment regimen. Several days later, he follows up for routine blood work and reports feeling well with no adverse reactions. Blood work reveals a creatinine of 1.6 mg/dL (baseline 1.0 mg/dL), and a urinalysis shows hematuria, pyuria, and crystalluria.

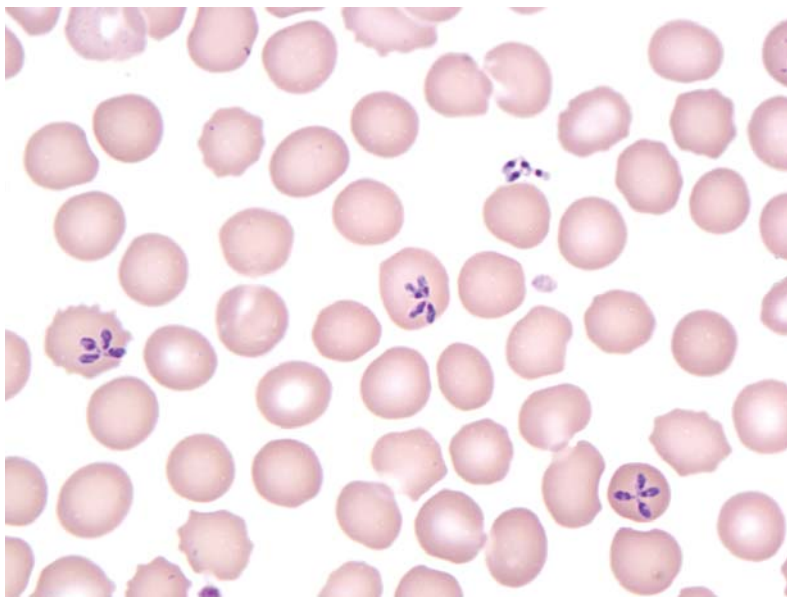
Which of the following medications is most likely responsible?

- (A) Tenofovir
- (B) Abacavir
- (C) Indinavir
- (D) Efavirenz
- (E) Maraviroc
- (F) Didanosine

**The answer is C: Indinavir.** Crystal nephropathy is a potential adverse reaction of indinavir, a protease inhibitor used in the treatment of HIV. Other

protease inhibitors can cause crystalluria, but indinavir has a high incidence of this complication. Additional medications that can cause crystal nephropathy include methotrexate, acyclovir, and ethylene glycol. (A) Tenofovir is a nucleoside reverse transcriptase inhibitor (NRTI) that can cause renal failure, but the mechanism is not by crystal formation within the tubules. (B) Abacavir is another NRTI that has a high incidence of life-threatening hypersensitivity reactions, especially in patients who are HLA-B\*5701 positive. (D) Efavirenz is nonnucleoside reverse transcriptase inhibitor (NNRTI) that causes depression and other CNS effects. (E) Maraviroc antagonizes CCR5 and inhibits entry of HIV into host cells; it can cause hepatotoxicity. (F) Didanosine is an NRTI, and like other NRTIs it may cause lipodystrophy and lactic acidosis.

- 10** A 48-year-old man presents to the Emergency Department with fevers, headache, fatigue, and yellowing of his skin and eyes. The constitutional symptoms began 3 days ago, and he thought it was the flu. This morning, his girlfriend noticed that his eyes appeared yellow. He has a history of hypertension and Graves disease, which are both stable. The patient lives in rural New York and is a nature photographer. He has no pets and does not smoke. Initial laboratory values are significant for a hemoglobin of 9.6 mg/dL, a serum leukocyte count of  $14,500/\text{mm}^3$ , and a serum lactate dehydrogenase of 210 U/L. His peripheral blood smear is shown in Figure 6-4.



**Figure 6-4**



Which of the following is the most likely diagnosis?

- (A) *Plasmodium falciparum*
- (B) *Strongyloides stercoralis*
- (C) *Clonorchis sinensis*
- (D) *Echinococcus granulosus*
- (E) *Ehrlichia chaffeensis*
- (F) *Borrelia burgdorferi*
- (G) *Rickettsia rickettsii*
- (H) *Babesia microti*

**The answer is H: *Babesia microti*.** Babesiosis is caused by the parasite *Babesia microti*, which is carried by *Ixodes* ticks. Patients often present with nonspecific flu-like symptoms and a hemolytic anemia, which is indicated by this patient's low hemoglobin and high serum lactate dehydrogenase. The peripheral blood smear shows the parasites within RBCs, confirming the diagnosis. If merozoites are present within RBCs, a "Maltese cross" pattern is seen. Treatment is with azithromycin and atovaquone in mild cases, or quinine and clindamycin in severe cases.

(A) *Plasmodium falciparum* causes malaria and should be considered since it also infects RBCs and produces fever and hemolytic anemia. (B) *Strongyloides* is a nematode and one of the most common parasitic infections worldwide. Infection occurs within the small intestine and can cause intestinal obstruction requiring surgery. (C) *Clonorchis sinensis* is a liver fluke that resides in the biliary tract and can cause obstructive jaundice; however, it does not produce intraerythrocytic inclusions. (D) *Echinococcus granulosus* is a tapeworm that typically causes disease of the lung and liver. It can cause liver cysts, which should not be biopsied (if possible) given the risk of a subsequent anaphylactic reaction. (E) Ehrlichiosis is also a tick-borne infection but is caused by gram-negative bacteria and does not cause RBC inclusions. (F) *B. burgdorferi* is a spirochete that causes Lyme disease, which manifests acutely with a flu-like illness and erythema migrans. (G) *R. rickettsii* causes Rocky Mountain spotted fever, but this patient does not have a rash.

11

A 63-year-old man presents to his physician due to persistent fevers. He says that he initially saw a physician for a fever about a month ago, and the workup was negative. He did not receive antibiotics at that time. Since then, he has measured his temperature at home and has had temperatures higher than 38.5°C. He denies any headache, cough, shortness of breath, abdominal pain, jaundice, bone or muscle pain, body swelling, or other concerning symptoms. He is otherwise healthy and sees the physician annually, receiving all necessary screening procedures. He has not traveled recently and has had no sick contacts or animal exposures. On physical examination, a new murmur is heard over the cardiac apex, but the rest of the examination, including assessment of skin and lymph nodes, is unremarkable. Three sets of

blood cultures are sent to the laboratory and later return negative. An echocardiogram is performed and shows a vegetation on the mitral valve. Other significant laboratory values include a hemoglobin of 12.4 g/dL, a leukocyte count of 11,500/mm<sup>3</sup>, and negative testing for ANA and antiphospholipid antibodies.

Which of the following is the likely cause of this patient's recurring fevers?

- (A) Malignancy
- (B) Verrucous endocarditis
- (C) Infective endocarditis
- (D) Large artery vasculitis

**The answer is C: Infective endocarditis.** This patient meets the definition of fever of unknown origin (FUO), which requires recurring fevers >38.3°C for ≥3 weeks, with a failed attempt to make a diagnosis. Many cases remain undiagnosed; however, this patient has a new murmur on cardiac examination and a valvular vegetation on echocardiography. Though blood cultures are often positive in patients with endocarditis, there are certain organisms that can produce culture-negative infective endocarditis. *Coxiella*, *Bartonella*, and *Streptococcus* species are the most common causes. The HACEK organisms were previously thought to be the most common cause of culture-negative endocarditis; however, current blood culture techniques can isolate many of these organisms after 3 to 5 days.

A full workup for FUO includes many blood tests, urine studies, cultures from multiple sites, and imaging studies, but knowing the details of this workup is not high yield for the shelf examination. Just consider the main etiologic categories for FUO, and the details of the vignette usually indicate the diagnosis. (A) Malignancy is always a concern in a patient with FUO, with common examples including leukemia, lymphoma, renal cell carcinoma, and abdominal cancers. (B) Verrucous endocarditis (Libman–Sacks endocarditis) will also present with negative blood cultures and is usually asymptomatic; it is associated with systemic lupus erythematosus (SLE) and the antiphospholipid syndrome; however, the negative tests for ANA and antiphospholipid antibodies rule out these diagnoses. (D) Vasculitides and other connective tissue diseases are causes of FUO, but these diagnoses are not suggested by the vignette. Though the clinical presentations vary considerably, findings that would suggest a vasculitis include palpable purpura, pulmonary and/or renal involvement, and asymmetric polyneuropathy. Other important causes of FUO include infections (e.g., TB, osteomyelitis, viral infections; always consider infections in HIV patients), thrombosis (e.g., deep venous thrombosis), and factitious fever.



12 A 54-year-old woman with a history of rheumatoid arthritis and hypertension presents to the Emergency Department with a high fever and headache. The symptoms began last night and were worse this morning. She also complains of severe sensitivity to light. Her medications

include hydrochlorothiazide and methotrexate. She denies any cough, weight loss, chest pain, shortness of breath, or abdominal pain, and she has no history of chronic headaches or neurologic disease. Her temperature is 39.5°C, blood pressure is 146/90 mmHg, heart rate is 88 beats per minute, and respiratory rate is 14 breaths per minute. She is somewhat confused, and there is significant nuchal rigidity and her headache becomes worse when she moves her head quickly to the side. The neurologic examination, including a cranial nerve examination, is unremarkable. A fundoscopic examination shows bilateral blurring of the optic disk margins and retinal venous engorgement.

Which of the following should be performed next in the workup of this patient?

- (A) CT scan
- (B) MRI
- (C) Lumbar puncture
- (D) Administer empiric antibiotics

**The answer is A: CT scan.** The suspected diagnosis here is meningitis, and a CT scan should be performed first to rule out mass effect before a lumbar puncture is performed. She has a high fever, as well as other symptoms/signs of meningitis (including the most sensitive test for meningitis: the jolt accentuation sign, in which a patient's headache intensifies after a quick head jolt). Kernig (pain and resistance with knee flexion while the hips are flexed at 90 degrees) and Brudzinski (involuntary flexion of hips and/or knees with passive neck flexion) signs are not sensitive, but they are fairly specific.

Once a diagnosis of meningitis is suspected and a lumbar puncture needs to be performed, a CT scan should be performed in patients thought to be at high risk for cerebral herniation. Risk factors include papilledema, previous CNS disease, a seizure in the past week, immunosuppression, altered mental status, and focal neurologic signs. (C) This patient has both papilledema and immunosuppression (methotrexate), and therefore, a CT scan should be performed before a lumbar puncture to assess the risk for cerebral herniation during lumbar puncture. (B) An MRI provides better visualization of the brain; however, it is costly and time-consuming. Because the purpose here is to rule out mass effect, a CT scan can do this adequately and quickly. (D) It is most appropriate to administer empiric antibiotics shortly after blood and CSF cultures are sent; however, the lumbar puncture has not been performed yet.



13

A 33-year-old woman presents with a chief complaint of abdominal pain. The pain is epigastric and is worse with meals. It is associated with nausea, a burning sensation, and bloating. She denies any weight loss, vomiting, and bloody or dark stools. She has no other medical problems and takes no medications. She denies recent NSAID use or heavy alcohol consumption. An upper endoscopy is performed, which shows several gastric ulcers and one duodenal ulcer. Biopsy confirms infection with *Helicobacter pylori*.

What is the most appropriate treatment at this time?

- (A) Amoxicillin, metronidazole, and bismuth
- (B) Amoxicillin, clarithromycin, and omeprazole
- (C) Lansoprazole, bismuth, metronidazole, and tetracycline
- (D) Symptomatic treatment with antacids

**The answer is B: Amoxicillin, clarithromycin, and omeprazole.** This patient presents with symptoms of dyspepsia and is found to have peptic ulcer disease (PUD) on endoscopy. Although there are other causes of gastric ulcers, *H. pylori* is the most common cause and should be treated when present. Triple therapy is the most common method of treatment and involves the use of clarithromycin, amoxicillin (an alternative is metronidazole), and a proton pump inhibitor for 10 to 14 days. (A) Metronidazole is an alternative to amoxicillin, so using both together without clarithromycin is not effective. (C) Quadruple therapy is unnecessary in most patients and should be used for resistant strains of *H. pylori* or if the patient is allergic to amoxicillin. (D) *H. pylori* eradication is the standard of care for PUD.

- 14** A 43-year-old woman presents to her physician for severe joint pain affecting her hands, elbows, and left knee. She has no other medical problems and works as a medical assistant at a local prison. On examination, the metacarpophalangeal joints of both hands are swollen and erythematous. Blood work reveals a positive rheumatoid factor. She elects to begin treatment with a disease-modifying antirheumatic drug



**Figure 6-5**

(DMARD). Several weeks later, the patient has an improvement of the pain in her joints but now complains of fever, chills, and a productive cough. Her chest x-ray is shown in *Figure 6-5*.

Which of the following represents the mechanism of action of this patient's medication?

- (A) Binds CD20 on the surface of B-cells
- (B) Binds and inhibits the effects of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )
- (C) Competitively inhibits dihydrofolate reductase
- (D) Nonselectively inhibits both cyclooxygenase-1 and -2 (COX-1, -2)

**The answer is B: Binds and inhibits the effects of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ).** The patient's chest x-ray is concerning for reactivation TB, which is indicated by the apical infiltrate with cavitation. Both her job as a healthcare worker and her exposure to jail inmates place her at risk for TB. Reactivation of latent TB is a known complication of TNF- $\alpha$  inhibitors used in the treatment of rheumatoid arthritis and other autoimmune diseases, and therefore the standard of care is to screen for latent TB before initiating one of these medications. TNF- $\alpha$  is released by activated macrophages and helps maintain the granuloma structure through signaling to surrounding lymphocytes. Agents that inhibit the actions of TNF- $\alpha$  include infliximab, adalimumab, etanercept, golimumab, and certolizumab pegol. Although many of the other medications in the answer choices cause immunosuppression, which is a risk factor for reactivation of latent TB, the risk is much greater in TNF- $\alpha$  inhibitors and therefore **B** is the best answer. (**A**, **C**, **D**) These answer choices reflect the mechanisms of rituximab, methotrexate, and NSAIDs, respectively. Both rituximab and methotrexate are DMARDs.

15

A 32-year-old mailman presents to the Emergency Department with the development of fever and shortness of breath over the past day. He denies any sick contacts or abnormal exposures and was previously well with no past medical history. He is tachycardic and tachypneic, and a chest x-ray of his lungs shows mediastinal widening and bilateral pleural effusions.

Which of the following is the most likely responsible organism?

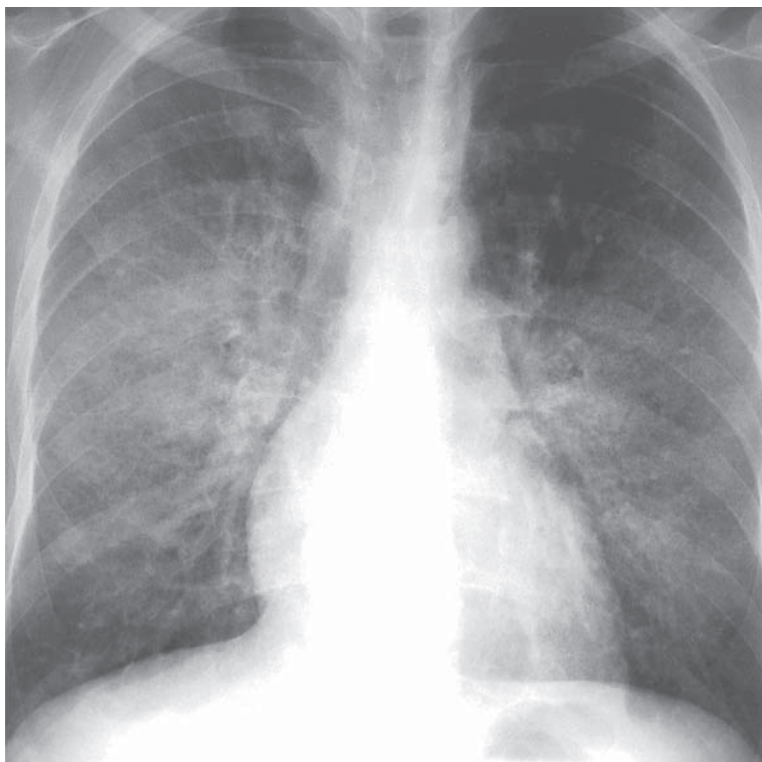
- |                                     |                                    |
|-------------------------------------|------------------------------------|
| (A) <i>Streptococcus pneumoniae</i> | (G) <i>Clostridium botulinum</i>   |
| (B) <i>Staphylococcus aureus</i>    | (H) <i>Clostridium perfringens</i> |
| (C) <i>Pseudomonas aeruginosa</i>   | (I) <i>Bacillus anthracis</i>      |
| (D) <i>Legionella pneumophila</i>   | (J) <i>Haemophilus influenzae</i>  |
| (E) Influenza virus                 | (K) <i>Francisella tularensis</i>  |
| (F) <i>Yersinia pestis</i>          | (L) <i>Coxiella burnetii</i>       |

**The answer is I: *Bacillus anthracis*.** The acute onset of a pulmonary syndrome with mediastinal widening and pleural effusions is concerning for a bioterrorism agent, and *B. anthracis* is the most likely organism responsible. The CDC lists anthrax as a very likely bioterrorism agent to be used given its very high mortality rate, ease of use, and durability of the spores. It can be released in the mail (as was done in 2001, killing 5), or released into the food, water, or air (e.g., cropduster planes). Infection is indicated by the affected system (pulmonary, GI, and cutaneous anthrax), and pulmonary anthrax has the highest mortality.

(A, B, J) *S. pneumoniae*, *S. aureus*, and *H. influenzae* may cause CAP, but would not show mediastinal widening on chest x-ray. (C) *Pseudomonas* is a common cause of HAP. (G, H) *C. botulinum* can cause a severe flaccid paralysis, and *C. perfringens* can cause both food poisoning and gas gangrene. (D, E, F, K, L) These are potential bioterrorism agents that cause respiratory symptoms; however, mediastinal widening is consistent with anthrax and not these other infections. *Legionella* causes Legionnaires' disease (or the less severe Pontiac fever), which presents with symptoms of pneumonia, confusion, relative bradycardia (low for what the heart rate should be in the presence of fever), hyponatremia, and renal/hepatic abnormalities on laboratory values. Influenza causes significant morbidity and mortality in those at risk (e.g., immunosuppressed, elderly), and will show bilateral interstitial or alveolar infiltrates if it affects the lungs. *Y. pestis* causes the bubonic plague, which presents with sudden painful lymphadenopathy and bilateral infiltrates in the cause of pneumonic plague. *F. tularensis* causes tularemia, which can present in different ways based on the infected system. If the lungs are infected, it can produce hemorrhagic inflammation with bilateral infiltrates and hilar adenopathy on chest x-ray. *C. burnetii* causes Q fever, which presents not only with mild respiratory symptoms (i.e., nonproductive cough) but also with high fever, headache, myalgias, vomiting, diarrhea, abdominal pain, and/or chest pain.

16

A 48-year-old man presents to the hospital with shortness of breath. He was diagnosed with HIV 2 years ago, refused treatment, and was lost to follow-up. Now he has developed a fever with severe shortness of breath. He has no other known medical problems and takes no medications. He is allergic to sulfa drugs and develops a severe skin rash. His family history is negative for cardiac or pulmonary disease. On examination, his temperature is 38.4°C, blood pressure is 120/80 mmHg, heart rate is 104 beats per minute, respiratory rate is 32 breaths per minute, and oxygen saturation is 84% on room air. An arterial blood gas is significant for a PaO<sub>2</sub> of 60 mmHg and a PaCO<sub>2</sub> of 28 mmHg. Sputum and blood cultures, as well as other laboratory tests, are pending. The patient's chest x-ray is shown in Figure 6-6.



**Figure 6-6**

What is the most appropriate management of this patient?

- (A) Ampicillin-sulbactam and clarithromycin
- (B) Trimethoprim-sulfamethoxazole
- (C) Vancomycin, levofloxacin, and piperacillin-tazobactam
- (D) Pentamidine
- (E) Prednisone and then atovaquone

**The answer is E: Prednisone and then atovaquone.** This patient presents with untreated HIV and likely has a low CD4 count at this time. Patients with CD4 counts below 200 should begin prophylaxis for *Pneumocystis jirovecii* pneumonia (PCP) with trimethoprim-sulfamethoxazole. Because this patient has a sulfa allergy, alternative treatments include dapsone, pentamidine, or atovaquone. This patient was not taking any prophylaxis and has likely developed PCP, which is indicated by the bilateral interstitial infiltrates on chest x-ray. For patients with a  $\text{PaO}_2 < 70$  mmHg or an A-a gradient  $> 35$  mmHg, it is



beneficial to treat them with prednisone before antibiotics to reduce the severe inflammatory response to the dying pathogens. (B) Since he has a sulfa allergy, he should not be treated with trimethoprim-sulfamethoxazole; an appropriate alternative treatment is prednisone followed by atovaquone.

(A, C) Ampicillin-sulbactam and clarithromycin are empiric antibiotics for inpatient management of CAP, and the combination of vancomycin, levofloxacin, and piperacillin-tazobactam is a broad spectrum antibiotic regimen used for the treatment of CAP requiring ICU level care. (D) Pentamidine is an alternative to trimethoprim-sulfamethoxazole, but steroids should also be given.



17 A 23-year-old man with a history of cystic fibrosis presents to the Emergency Department in respiratory failure. He is found to be febrile with leukocytosis and infiltrates on chest x-ray. Sputum Gram stain shows gram-negative rods, and culture grows oxidase-positive colonies that produce a sweet smell. Other significant laboratory values include a leukocyte count of  $17,300/\text{mm}^3$  and a creatinine of 1.6 mg/dL (baseline 0.9 mg/dL).

Which of the following is the most appropriate antibiotic for this patient?

- (A) Gentamicin
- (B) Cefepime
- (C) Vancomycin
- (D) Cephalexin

**The answer is B: Cefepime.** *Pseudomonas* is a common respiratory infection in cystic fibrosis patients and is a major cause of mortality. It is a common nosocomial pathogen, seen in many cases of HAP and VAP, and is often MDR. It is also a common infectious agent in any immunocompromised patient, especially in burn and neutropenic patients. For the shelf examination, it is important to know antibiotic coverage for two common MDR pathogens: *Pseudomonas* and MRSA. Appropriate antibiotics for *Pseudomonas* are based on culture and sensitivity data, but commonly used agents include certain  $\beta$ -lactams (piperacillin-tazobactam, ticarcillin-clavulanate, cefepime, ceftazidime, and all carbapenems except for ertapenem), fluoroquinolones (levofloxacin, ciprofloxacin), aminoglycosides (gentamicin, amikacin, tobramycin), aztreonam (a monobactam that can be used in patients allergic to penicillin), and colistin. (C) The choice of antibiotic for MRSA depends on the type of infection and whether the infection is community acquired or hospital acquired; common agents for serious infections include vancomycin, daptomycin, clindamycin, linezolid, ceftaroline, telavancin, and tigecycline. Vancomycin is typically given as an answer choice for treating suspected MRSA.

(A) Aminoglycosides are not the *best* agent for this patient for two reasons: First, aminoglycosides are not the preferred drugs to treat pneumonia; second, the patient is suffering from acute kidney injury and aminoglycosides have a high rate of nephrotoxicity. (D) Cephalexin has no activity against *Pseudomonas*.



18

A 63-year-old woman with a history of poorly controlled diabetes, hypertension, and coronary artery disease presents to her physician complaining of worsening shortness of breath, fevers, back pain, and cough. The symptoms developed slowly over the past month, and she claims to be extremely fatigued due to an inability to sleep at night from fevers and night sweats. She previously worked as a nurse but is now retired. She drinks alcohol moderately and does not smoke. She has had all of her recommended screening procedures, which have been unremarkable. On examination, she is febrile to  $38.6^{\circ}\text{C}$  with a blood pressure of 118/82 mmHg, a heart rate of 92 beats per minute, and a respiratory rate of 24 breaths per minute. Her laboratory values are shown below.

|                            |                         |
|----------------------------|-------------------------|
| Hemoglobin                 | 10.8 g/dL               |
| Leukocyte count            | 9,400/mm <sup>3</sup>   |
| Platelets                  | 325,000/mm <sup>3</sup> |
| Sodium                     | 132 mEq/L               |
| Potassium                  | 3.9 mEq/L               |
| Creatinine                 | 0.9 mg/dL               |
| Glucose                    | 186 mg/dL               |
| Aspartate aminotransferase | 64 U/L                  |
| Alanine aminotransferase   | 60 U/L                  |
| Alkaline phosphatase       | 146 U/L                 |

An ECG shows Q waves that are unchanged from her previous ECGs, and a chest x-ray shows diffuse reticulonodular infiltrates in both lungs.

Which of the following is the most likely diagnosis?

- (A) Congestive heart failure
- (B) Disseminated TB
- (C) Metastatic colorectal cancer
- (D) HIV infection with PCP

**The answer is B: Disseminated TB.** Although diagnosing TB can be difficult given its large variety of clinical manifestations, there are certain findings that suggest this as the correct diagnosis. Disseminated TB (miliary TB) commonly presents in a subacute/chronic, indolent fashion, although it can present acutely with septic shock and acute respiratory distress syndrome

(ARDS). Risk factors for dissemination include immunosuppression, increasing age, diabetes mellitus, and alcoholism, and this patient is older with poorly controlled diabetes and a history of likely exposure to TB (given her occupation as a nurse). The natural course of TB is summarized in *Figure 6-7*.

Common manifestations of disseminated disease include systemic symptoms (fever, chills, night sweats, weight loss), pulmonary disease (pattern of small “millet seed” opacities in the lungs), bone and joint involvement (e.g., vertebral osteomyelitis in Pott disease), lymphadenitis, liver involvement, peritonitis, and many other manifestations based on the organ affected. Common laboratory findings in miliary TB include anemia, hyponatremia, elevated liver enzymes, and elevated alkaline phosphatase. Other useful diagnostic tests in this patient would be an acid-fast smear and culture of the sputum, purified protein derivative (PPD; though anergy leading to false negatives is common in miliary TB) or interferon- $\gamma$  release assay, and further imaging (e.g., spinal MRI to assess for Pott disease given her complaint of low back pain). (Note: If the diagnosis is difficult to make, other supportive findings include granulomas on biopsy and an elevated adenosine deaminase in certain body fluids [e.g., ascites, pleural effusion].)

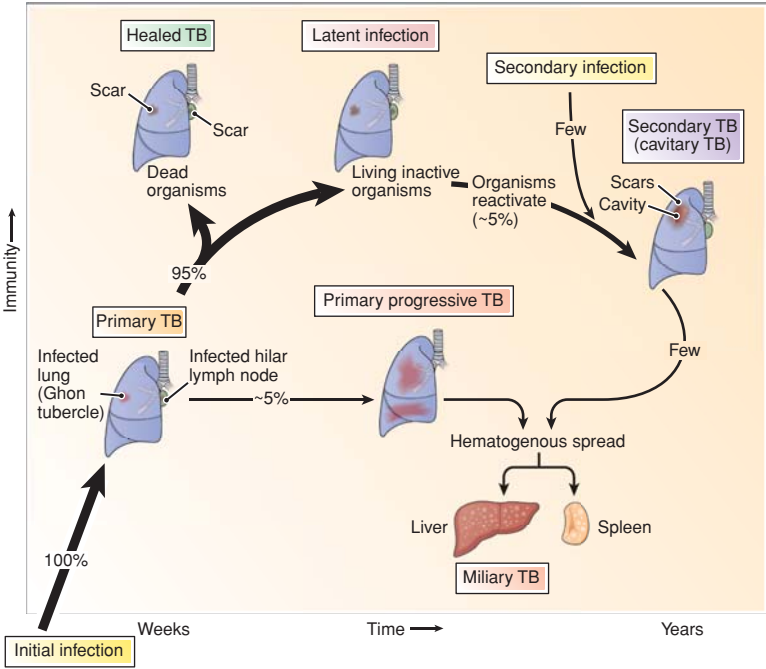


Figure 6-7

(A) Though the patient has a history of coronary artery disease and is experiencing shortness of breath, the presence of fever suggests an inflammatory process. (C) The patient has constitutional symptoms and anemia that may be seen with colorectal cancer, but the findings on chest x-ray support the diagnosis of miliary TB; metastases to the lungs do not produce a diffuse reticulonodular appearance. The vignette also mentions that her screening procedures (e.g., colonoscopy) have been normal. (D) PCP may produce bilateral interstitial infiltrates on chest x-ray, but the presence of other organ involvement (back pain, transaminitis) suggests an alternative diagnosis.

**19** A 39-year-old woman complains of fever, cough, and shortness of breath. She is from Missouri and lives on a farm with her husband and two children. She has never smoked and does not drink alcohol or use illicit drugs. Her temperature is 38.2°C, blood pressure is 112/70 mmHg, heart rate is 90 beats per minute, and respiratory rate is 26 breaths per minute. There are scattered wheezes and rales on pulmonary auscultation, and there are tender, erythematous nodules on the anterior portion of her legs bilaterally. A chest x-ray shows pulmonary infiltrates and hilar lymphadenopathy. A urine antigen test is performed and returns positive, confirming the diagnosis.

What is the most likely diagnosis?

- (A) Tuberculosis
- (B) Hypersensitivity pneumonitis
- (C) Sarcoidosis
- (D) Histoplasmosis
- (E) Coccidioidomycosis

**The answer is D: Histoplasmosis.** Pulmonary histoplasmosis is one manifestation of infection due to *Histoplasma capsulatum*, which primarily affects people in the Ohio and Mississippi River valleys. Pulmonary infection may be subclinical, but can also cause a severe pneumonia with cavitations, pulmonary nodules, and mediastinal and hilar lymphadenopathy. In immunosuppressed patients, the infection can disseminate and cause fever, skin and oral lesions, hepatosplenomegaly, lymphadenopathy, fibrosing mediastinitis, pericarditis, and other findings. This patient has features of pulmonary histoplasmosis and erythema nodosum, which is associated with histoplasmosis. A urinary antigen test is one method of diagnosing histoplasmosis, and treatment is with itraconazole.

(A) Histoplasmosis can mimic TB, especially in the chronic form that manifests as fevers, weight loss, night sweats, and apical infiltrates on chest x-ray. There are no risk factors for TB mentioned in the vignette, and the patient is from an area endemic for histoplasmosis. (B) While this diagnosis may be considered given that she lives on a farm (“farmer’s lung”), it is not diagnosed with a urine antigen test. (C) Sarcoidosis also commonly involves the lungs and causes hilar

lymphadenopathy, but is not diagnosed with a urinary antigen test. Misdiagnosing this patient with sarcoidosis would have disastrous consequences, since the treatment of sarcoidosis is immunosuppression that could cause dissemination of the infection. (E) *Coccidioidomycosis* also causes pulmonary disease, but affects people in the Southwestern United States. An overview of the important fungal infections and the organs to which they disseminate is shown in *Figure 6-8*.

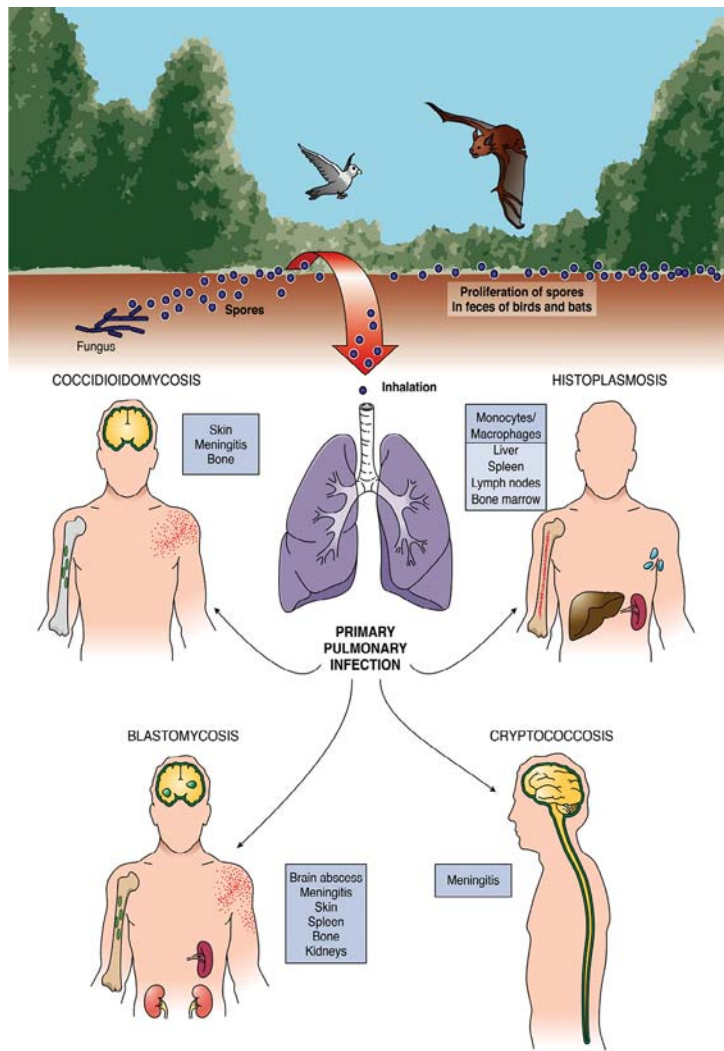


Figure 6-8

20

A 32-year-old woman presents to her physician because of vaginal discharge. She is sexually active and uses barrier protection inconsistently. After some tests, she is diagnosed with *Chlamydia trachomatis* cervicitis. A pregnancy test is also performed, which is negative.

The medication used to treat this patient works by which of the following mechanisms?

- (A) Inhibition of peptidoglycan cross-linking
- (B) Inhibition of dihydropteroate synthase
- (C) Inhibition of DNA topoisomerases
- (D) Protein synthesis inhibition by blocking the 30S ribosomal subunit
- (E) Inhibition of initiation complex formation

**The answer is D: Protein synthesis inhibition by blocking the 30S ribosomal subunit.** A first-line treatment choice for *Chlamydia* infection is doxycycline, a tetracycline antibiotic that blocks translation by binding the bacterial 30S ribosomal subunit. Another correct answer choice would be protein synthesis inhibition by blocking the 50S ribosomal subunit, since azithromycin (a macrolide antibiotic) is also an appropriate agent for treating *Chlamydia* infections. The remaining answer choices reflect the mechanism of (A)  $\beta$ -lactam antibiotics; (B) sulfonamides; (C) fluoroquinolones; and (E) aminoglycosides.

21

A 26-year-old woman presents to her physician with multiple complaints. Two days ago, she noticed fevers, chills, and malaise. One day ago, she developed pain in her left knee, left ankle, and right elbow; in addition, there is pain and swelling over her hands. She denies any other medical problems, recent upper respiratory tract infections or diarrheal illnesses, and does not smoke or use illicit drugs. She is sexually active and has had several new partners in the last few months. She is examined, which is significant for pain to palpation over the tendons in her hand and wrist, multiple scattered hemorrhagic vesicles and pustules over the dorsal aspects of both forearms, and erythema and swelling of her left knee, left ankle, and right elbow with decreased range of motion at these joints.

Which of the following is the most likely diagnosis?

- (A) Reactive arthritis
- (B) Infective endocarditis
- (C) Disseminated *Neisseria gonorrhoeae*
- (D) *Neisseria meningitidis* infection

**The answer is C: Disseminated *Neisseria gonorrhoeae*.** This young, sexually active patient is presenting with systemic symptoms, tenosynovitis, pustular skin lesions, and polyarthritides, which suggests the diagnosis of disseminated gonococcal infection. This infection can present with the symptoms seen in this vignette, or with purulent arthritis without cutaneous manifestations.

Diagnosis can be confirmed with blood cultures, cervical cultures, or synovial fluid analysis, and treatment is with ceftriaxone.

(A) Reactive arthritis may develop in response to a diarrheal illness or a *Chlamydia trachomatis* infection; it can also present with oligoarthritis but also commonly presents with uveitis and urethritis. Reactive arthritis is less likely to have cutaneous manifestations. (B) There is no mention of a cardiac murmur, and this patient does not meet the modified Duke criteria for the diagnosis of infective endocarditis. (D) *N. meningitidis* infection can present similarly, but typically has more severe systemic symptoms (with or without meningitis).

22

A 47-year-old man with no significant medical history presents to the Emergency Department after suffering his first seizure. He says that he has had headaches for the past week and has not felt

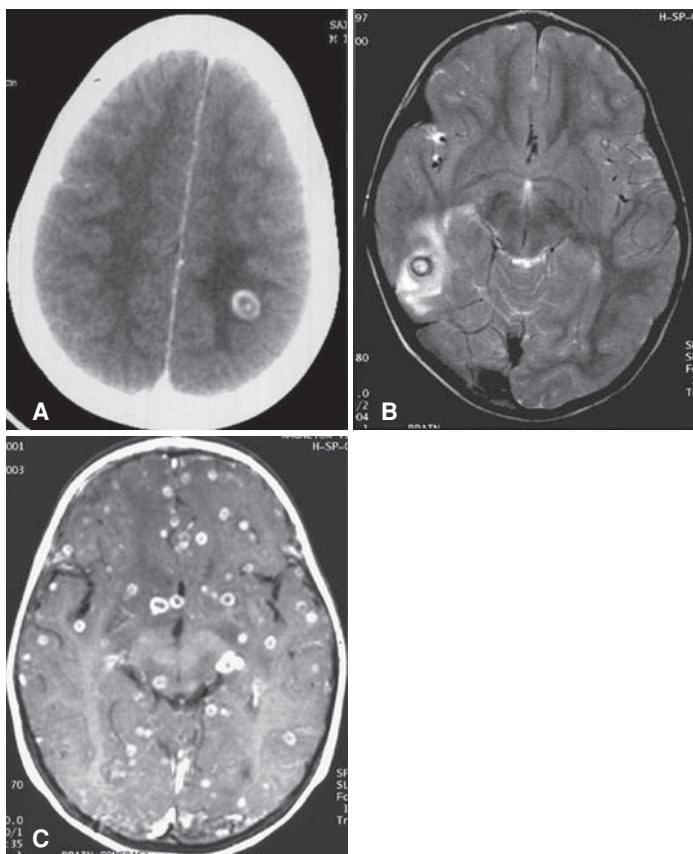


Figure 6-9

himself. He lives with his family in California, and his mother recently moved in with him after immigrating to the United States from El Salvador. He is afebrile with normal vital signs, and a brief screening physical examination is normal. He is currently alert and oriented to person, place, and time. An MRI of the brain is shown in Figure 6-9.

What is the most appropriate treatment for this patient?

- (A) Albendazole, dexamethasone, and levetiracetam
- (B) Praziquantel
- (C) Pyrimethamine-sulfadiazine
- (D) Vancomycin
- (E) Amphotericin B

**The answer is A: Albendazole, dexamethasone, and levetiracetam.**

The brain imaging above shows a scolex (first two images) and many non-enhancing cysts with surrounding edema (third image). A scolex within the cyst cavity is pathognomonic for neurocysticercosis, one of the manifestations of infection by the pork tapeworm *Taenia solium*. Neurocysticercosis is the most common cause of seizure in Central America, and this patient's mother recently immigrated from El Salvador. Neurocysticercosis is *not* caused by ingesting infected pork; those who eat infected pork become *carriers* of cysticercosis, but do not develop disseminated cysticercosis (e.g., neurocysticercosis). It is only by ingesting eggs shed in the carrier's feces (e.g., fecal contamination of food) that one develops neurocysticercosis, since it is the embryos that hatch from the eggs that disseminate hematogenously. Treatment is with an antiparasitic agent (e.g., albendazole or praziquantel), and a corticosteroid should be added to reduce inflammation in response to the dying pathogens. (B) Because the patient presented with a seizure, an antiepileptic medication should be started in addition to an antiparasitic medication and a corticosteroid. (Of note, antiparasitic medications are not necessary if there are calcified cysts with no viable parasites.)

(C) Pyrimethamine-sulfadiazine is the treatment for toxoplasmosis, which presents with ring-enhancing lesions on brain imaging. (D, E) Vancomycin and amphotericin B are typically used for MRSA and serious fungal infections, respectively, and are not used for neurocysticercosis.

**23**

A 29-year-old woman who is 18 weeks pregnant presents to her physician complaining of fever, cough, myalgias, and a skin rash (Figure 6-10). She has no other medical problems and has had regular prenatal care. Her only medication is a prenatal vitamin. She lives in a rural area of Minnesota and has not traveled recently or had any sick contacts.



Figure 6-10

What is the best treatment option for this patient?

- (A) Amoxicillin
- (B) Doxycycline
- (C) Erythromycin
- (D) Penicillin G

**The answer is A: Amoxicillin.** Lyme disease is caused by the spirochete *Borrelia burgdorferi*, which is carried by the *Ixodes* tick. Lyme disease is effectively prevented with removal of the tick within 24 hours. Clinical manifestations of the disease are based on the stage of disease. In the early stage, which occurs a few weeks after infection, there are nonspecific flu-like symptoms and an expanding erythematous rash with a central clearing called erythema migrans (Figure 6-10). After weeks to months, the disease can disseminate and cause migratory arthralgias, cutaneous annular lesions, cranial neuropathies, aseptic meningitis, cardiac conduction blocks, and other serious complications. The late stage of the disease, which occurs months to years after infection, manifests as arthritis and acrodermatitis chronica atrophicans (widespread skin atrophy with polyneuropathy).

(B) Treatment of Lyme disease is with doxycycline; however, this patient is pregnant and so doxycycline is contraindicated. Amoxicillin is the best alternative treatment in pregnant patients or those allergic to doxycycline. (C) Erythromycin is also teratogenic. A useful mnemonic for remembering teratogenic antibiotics is “SAFE Moms Take Really Good Care”: Sulfonamides, Aminoglycosides, Fluoroquinolones, Erythromycin, Metronidazole, Tetracyclines, Ribavirin, Griseofulvin, and Chloramphenicol. (D) Penicillin G is the treatment of *Treponema pallidum* (syphilis), another spirochete. A third medically important spirochete is *Leptospira*, which can cause a spectrum of disease ranging from a mild subclinical infection to life-threatening renal failure, ARDS, jaundice, and pulmonary hemorrhage (Weil disease).

A 38-year-old woman with no previous medical history presents to the Emergency Department with a fever and severe headache. She is not taking any medications and denies recent travel, sick contacts, or recent



illnesses. She lives in California and works as a secretary. She does not have any pets and has been sexually active exclusively with her husband for the past 18 years. Other than a temperature of 39.3°C, her vitals are within normal limits. She has some nuchal rigidity and her hips flex when her neck is flexed. There are no signs of papilledema on fundoscopic examination. A lumbar puncture is performed, and the results are shown below.

|                  |                                                 |
|------------------|-------------------------------------------------|
| Opening pressure | 100 mmH <sub>2</sub> O                          |
| Leukocytes       | 110/mm <sup>3</sup> (predominantly lymphocytes) |
| Total protein    | 65 mg/dL                                        |
| Glucose          | 82 mg/dL                                        |

A screening HIV test and blood cultures are negative, and Gram stain and cultures of the CSF are also negative.

What is the most likely cause of this patient's condition?

- (A) *Streptococcus pneumoniae*
- (B) *Mycobacterium tuberculosis*
- (C) *Treponema pallidum*
- (D) West Nile virus
- (E) *Cryptococcus neoformans*
- (F) Echovirus
- (G) Rheumatoid arthritis
- (H) Systemic lupus erythematosus

**The answer is F: Echovirus.** Aseptic meningitis is diagnosed by CSF studies that show meningeal inflammation (elevated leukocytes) with negative blood and CSF culture results. The most common cause of aseptic meningitis is a viral infection, and enteroviruses (echovirus, coxsackievirus, etc.) are the most common type. The CSF in viral meningitis will show elevated leukocytes (with a lymphocyte predominance), elevated total protein, and normal glucose and opening pressure. Other potential viruses include herpesviruses, adenovirus, HIV, mumps, and many more. (D) West Nile virus is a possibility, but is a less common cause of aseptic meningitis. In addition, this patient does not have any obvious mosquito exposures (recent hiking, outdoor activity, etc.), making the diagnosis less likely. Treatment of viral meningitis is supportive (unless it is caused by HSV, in which acyclovir should be given).

(A) *S. pneumoniae* is the most common cause of bacterial meningitis, which would typically present with a higher CSF leukocyte count with a neutrophil predominance, a higher total protein, and a low glucose; CSF Gram stain and culture should also be positive. Other important bacterial pathogens include rickettsial infections, *Borrelia burgdorferi*, *Coxiella*, and *Ehrlichia*. (B, C) TB

and syphilis can both produce aseptic meningitis, and both commonly have a low CSF glucose. There are no TB risk factors or sexual risk factors presented in the vignette, making these etiologies unlikely. (E) *Cryptococcus* is a common cause of meningitis in HIV patients; however, this patient's screening HIV test was negative. *Coccidioides* is another fungal organism that can cause aseptic meningitis and typically presents with a low CSF glucose like other fungal infections. (G, H) Autoimmune conditions such as rheumatoid arthritis, SLE, sarcoidosis, and others can cause aseptic meningitis, but other historical clues and physical examination findings would likely be present to suggest this as the diagnosis. Other important causes of aseptic meningitis include neoplasms, medications (including NSAIDs, intravenous immunoglobulins, and trimethoprim-sulfamethoxazole), brain abscesses or partially treated bacterial meningitis, and parasites (e.g., toxoplasmosis).

25

A 62-year-old man is hospitalized for severe fatigue, fevers, and weight loss. He has no past medical history and takes no medications. His family history is negative for cardiac disease or cancer, and he does not smoke or drink alcohol. On examination, his temperature is 38.5°C with a normal blood pressure and heart rate. There is no scleral icterus, and he has good dentition. Cardiac auscultation reveals an early diastolic decrescendo murmur at the left upper sternal border. The pulmonary and abdominal examinations are normal. His laboratory values show a creatinine of 1.8 mg/dL (baseline 1.0 mg/dL), and his urinalysis shows WBCs and dysmorphic RBCs. His urine cultures are negative, but his blood cultures are positive for group D *Streptococcus*, specifically *Streptococcus gallolyticus*. The patient undergoes transthoracic echocardiography (TTE), which shows a vegetation on the aortic valve, and he begins treatment with penicillin G.

What should be done next in the management of this patient?

- (A) Transesophageal echocardiogram (TEE)
- (B) Colonoscopy
- (C) CT scan of the chest
- (D) Valvular surgery
- (E) Stop penicillin and start doxycycline

**The answer is B: Colonoscopy.** This patient meets the modified Duke criteria (Table 6-2) for infective endocarditis, since he has a new regurgitant murmur and positive blood cultures for an organism known to cause endocarditis. Both the viridans group of *Streptococcus* species as well as the *S. bovis* biotypes (note that nomenclature has changed; species include *S. gallolyticus* and *S. infantarius*) are common organisms that cause native valve endocarditis, even in patients without risk factors. The *S. bovis* biotypes are normal GI tract inhabitants and have been associated with colorectal cancer (especially *S. gallolyticus*). Patients who have positive blood cultures for this organism should also undergo colonoscopy given the association with colon cancer.

**Table 6-2 Modified Duke Criteria**

| Major                                                                                                                                                                                                                                                                                                                                                                   | Minor                                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• <b>Sustained bacteremia</b> by an organism known to cause endocarditis (or 1 BCx or (+) serology for <i>Coxiella</i>)<sup>a</sup></li> <li>• <b>Endocardial involvement</b> documented by <i>either</i> (+) <b>echocardiogram</b> (vegetation, abscess, prosthetic dehiscence) <i>or new valvular regurgitation</i></li> </ul> | <ul style="list-style-type: none"> <li>• Predisposing condition</li> <li>• Fever</li> <li>• <b>Vascular phenomena:</b> septic arterial or pulmonary emboli, mycotic aneurysms, ICH, Janeway lesions</li> <li>• <b>Immune phenomena:</b> (+) RF, GN, Osler nodes, Roth spots</li> <li>• (+) <b>BCx</b> not meeting major criteria</li> </ul> |
| <ul style="list-style-type: none"> <li>• Definitive (i.e., highly probable): 2 major <i>or</i> 1 major + 3 minor <i>or</i> 5 minor criteria</li> <li>• Possible: 1 major + 1 minor <i>or</i> 3 minor criteria</li> </ul>                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                             |

Se ~90%, Sp >95%, NPV ≥92% (Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis*. 2000;30(4):633–638.)

<sup>a</sup>Serologic or molecular tests for other known agents of Cx (–) endocarditis not yet included as major criterion, but may help diagnose.

BCx, blood culture; ICH, intracranial hemorrhage; RF, rheumatoid factor; GN, glomerulonephritis; Se, sensitivity; Sp, specificity; NPV, negative predictive value; Cx, culture.

Adapted from Sabatine M. *Pocket Medicine*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013.

(A) TEE would be appropriate if the TTE was nondiagnostic, or if it was negative and there was a high clinical suspicion for infective endocarditis. (C) CT scan of the chest is not part of the workup for infective endocarditis. (D) The indications for surgery to treat serious cases of infective endocarditis include CHF and cardiogenic shock, extension of the primary infection (e.g., periannular abscess), persistent embolic events despite treatment, difficult to treat organism, and prosthetic valve endocarditis (especially if there is valvular dysfunction). (E) Penicillin G is an appropriate treatment for group D strep infections. Antibiotic selection should be based on culture and sensitivity data, and most group D strep species are not sensitive to doxycycline.



A 58-year-old man is hospitalized for a severe COPD exacerbation that requires intubation.

Which of the following will reduce the risk of developing pneumonia in this patient?

- (A) Place the patient in a supine position
- (B) Avoid daily attempts to wean the patient from the ventilator
- (C) Administer oral chlorhexidine solution twice daily
- (D) Administer daily omeprazole
- (E) Avoid any instrumentation of the airway, including endotracheal suctioning

**The answer is C: Administer oral chlorhexidine solution twice daily.**

Mechanical ventilation is the biggest risk factor for developing HAP, and the risk can be decreased with certain measures. (A) Patient should be placed in a semirecumbent position (head of the bed elevated 30 to 45 degrees) to prevent aspiration events. (B) Daily attempts to wean a patient from the ventilator should be performed to minimize the duration of mechanical ventilation. (D) Omeprazole and other agents that increase the pH of gastric contents have been shown to increase the rate of HAP. They should be avoided if possible. (E) Endotracheal suctioning of subglottic secretions reduces the risk of VAP. Other important preventive measures include following proper hand hygiene protocols, avoiding gastric overdistention, and using orotracheal intubation rather than nasotracheal intubation.

**27** A 36-year-old man presents with fevers, chills, cough, and night sweats. The symptoms have developed over the past couple of weeks and have been associated with weight loss. His cough is productive of yellow sputum, and he occasionally is short of breath. The patient is originally from Botswana and currently works as a salesman. He does not smoke or use illicit drugs and has never been imprisoned. He is febrile on examination, with decreased breath sounds and rales in the upper lung field. A sputum AFB stain is positive, and his chest x-ray shows an apical infiltrate. He is started on a four-drug regimen. In addition, an HIV test is positive with a CD4 count of  $290/\text{mm}^3$  and he is started on antiretroviral therapy. Two weeks later, the patient follows up and reports feeling worse, with increased dyspnea. A repeat chest x-ray shows radiologic worsening of the prior pneumonia. A complete workup for a new source of infection is negative.

Which of the following diagnoses should be considered?

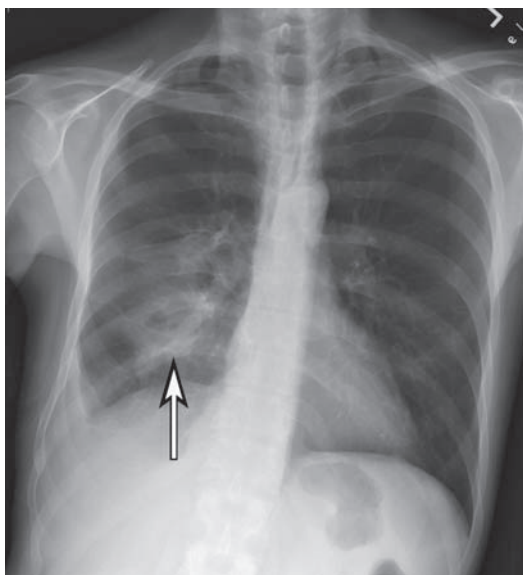
- (A) Allergic reaction to antiretrovirals
- (B) Immune reconstitution inflammatory syndrome
- (C) Secondary bacterial pneumonia
- (D) Rifampin toxicity

**The answer is B: Immune reconstitution inflammatory syndrome.** The immune reconstitution inflammatory syndrome (IRIS) occurs in patients who recently started antiretrovirals and have clinical deterioration; it is a diagnosis of exclusion. Because HIV and TB coinfection is common (especially in sub-Saharan African countries), there are many reported cases of IRIS that occur with appropriate TB treatment. Unless IRIS is severe, antiretrovirals can usually be continued. NSAIDs or corticosteroids may be added temporarily to reduce the inflammation and improve symptoms. (Of note, this patient has risk factors of drug-resistant TB, and treatment failure should also be considered; however, this was not an answer choice.)

(A) IRIS is not a result of an allergic reaction to HIV medications. (C) This patient has pulmonary TB, and although a secondary bacterial pneumonia is possible, this often occurs with lower CD4 counts (PCP is a common secondary infection). (D) Rifampin does not cause pulmonary toxicity.

28

A 49-year-old man presents to the Emergency Department complaining of fever and a productive cough for several weeks. He also endorses night sweats and perceived weight loss. The patient is homeless and is a known alcoholic. On examination, the patient's temperature is 38.3°C, blood pressure is 144/90 mmHg, heart rate is 94 beats per minute, and respiratory rate is 20 breaths per minute. He appears weak and disheveled with poor dentition. There are bronchial and amphoric breath sounds at the right lung base. His laboratory values are significant for a hemoglobin of 11.8 g/dL and a leukocyte count of 13,500/mm<sup>3</sup>. Blood and sputum cultures are collected and sent to the laboratory. His chest x-ray is shown in *Figure 6-11*.



**Figure 6-11**

What should be done next in the management of this patient?

- (A) Start itraconazole
- (B) Start clindamycin
- (C) Start vancomycin
- (D) Bronchoscopy and tissue biopsy
- (E) Surgical resection

**The answer is B: Start clindamycin.** There are many things that can cause a cavitory pulmonary lesion; however, this patient presents with a classic history for an anaerobic lung abscess secondary to aspiration. The diagnosis should be suspected in a patient at risk for aspiration (e.g., alcoholic with poor dentition) who presents with indolent symptoms/signs of a pulmonary infection, putrid sputum, and a cavitory pulmonary lesion in a dependent lung segment. Amphoric breath sounds (resonant, blowing sounds) are sometimes heard with auscultation over a cavitory lesion, but are not a consistent physical finding. Treatment with clindamycin is cheap and effective for anaerobic lung infections.

(A) This is the treatment for aspergillosis, which can also cause pulmonary necrosis and lung cavitation. However, chronic cavitory aspergillosis presents in patients with prior lung disease and usually occurs in the upper lobes. (C) Vancomycin is a good drug for MRSA if suspected; however, it would not be a good agent for monotherapy since this presentation suggests an anaerobic infection. In addition, clindamycin has some activity against MRSA. (D) Although sputum cultures are often difficult to interpret given the high rate of contamination, bronchoscopy is an invasive procedure; it should be performed if the sputum cultures are not diagnostic and if the patient fails to respond to empiric antibiotics. (E) Surgical intervention is rarely necessary and is a last resort for treatment.



A 32-year-old woman presents to her physician complaining of a productive cough for the past 2 weeks. She has not felt well and describes frequent production of yellow or green sputum. Her temperature is 37.5°C with a heart rate of 86 beats per minute and a respiratory rate of 18 breaths per minute. There are some scattered wheezes and rhonchi on auscultation of the lungs that clear with coughing, with no rales or dullness to percussion.

Which of the following is the most appropriate next step in management?

- (A) Start oseltamivir
- (B) Start ampicillin-sulbactam
- (C) Start albuterol inhaler as needed
- (D) Order sputum cultures
- (E) Order a chest x-ray
- (F) Education and symptom management

**The answer is F: Education and symptom management.** This patient has an acute cough lasting for 2 weeks without any vital sign abnormalities or evidence of pneumonia on lung auscultation, making the likely diagnosis acute bronchitis. (B, D) The vast majority of cases are caused by respiratory viruses (influenza, parainfluenza, RSV, adenovirus) and do not require sputum cultures or antibiotics. The patient should be educated about the risk of taking

unnecessary antibiotics and instructed to follow-up if symptoms persist. (E) If the symptoms persist for >3 weeks, or if there are any abnormal vital signs or physical examination findings suggestive of pneumonia, then a chest x-ray is warranted. (A) Oseltamivir is a neuraminidase inhibitor used for influenza A or B, but must be taken within 48 hours of symptom onset to have an appreciable effect. (C) There is no evidence that  $\beta_2$  agonists are beneficial in acute bronchitis, though they are often prescribed if there is significant wheezing on examination.



A 30-year-old medical student is undergoing medical screening in order to start a rotation at a new hospital. She denies any current symptoms and reports no previous medical problems. She is originally from South Africa and her vaccinations are up to date, including a *Bacillus Calmette–Guérin* (BCG) vaccine she received as a child. A PPD is placed and read 48 hours later, which shows an area of induration that is 11 mm wide.

What is the most appropriate next step in management?

- (A) Start rifampin, isoniazid, pyrazinamide, and ethambutol
- (B) Obtain a chest x-ray; if normal, reassure the patient
- (C) Obtain a chest x-ray; if normal, start isoniazid and pyridoxine for 9 months
- (D) Start isoniazid and pyridoxine for 9 months
- (E) Reassurance

**The answer is C: Obtain a chest x-ray; if normal, start isoniazid and pyridoxine for 9 months.** There are a couple of important teaching points in this vignette. First, screening for TB is often performed with a PPD, and it is important to know what the threshold is for a positive test result. In patients with close contact to a patient with active TB, a concerning chest x-ray, or who are immunosuppressed (via medications, HIV infection, etc.), a positive test is >5 mm. For those patients at high risk (healthcare workers, jail workers, the homeless, IV drug users, uncontrolled diabetes, chronic kidney disease, etc.), a positive test is >10 mm. And for all others without risk factors, a positive test is >15 mm. This patient has an induration of 11 mm and is a healthcare worker, therefore she warrants further workup to differentiate active from latent TB. (Note: Prior BCG vaccination rarely produces an induration of >10 mm as an adult, and the CDC recommends that BCG vaccination status should not influence the workup and treatment of TB.) If the chest x-ray is negative, then the patient has latent TB and should be treated within 9 months of isoniazid and pyridoxine (vitamin B<sub>6</sub>, which helps to prevent isoniazid-induced neuropathy).

(A) Treatment of active TB is becoming complicated with MDR-TB; however, active TB is generally treated with a four-drug regimen (rifampin, isoniazid, pyrazinamide, ethambutol) for 2 months followed up by a two-drug

regimen (rifampin, isoniazid) for 4 months. (B) Because this patient is a healthcare worker, she should be treated for latent TB given the risk of reactivation and exposure to other patients. (D) A chest x-ray should be performed before starting treatment to differentiate latent from active TB. (E) Reassurance would only be appropriate if the PPD result was negative.

31

A 45-year-old Caucasian man is referred for further workup of chronic abdominal pain and diarrhea. These symptoms have been present for 2 months, and he has lost 10 kg of weight over this time. He also reports that he has developed pain in multiple joints that comes and goes and seems to spread from one joint to the next. He denies fevers, chills, chest pain, shortness of breath, vomiting, episodes of constipation, or hematochezia. He is married and works as a farmer, with no recent sick contacts or travel. His vitals are within normal limits, and his examination is unremarkable. A complete laboratory workup is unremarkable. He undergoes a colonoscopy, which is normal, and then undergoes an upper endoscopy. Biopsy of the small intestine shows many macrophages within the lamina propria that stain positive with periodic acid-Schiff (PAS).

Which of the following is likely to cure this patient of his chronic diarrhea?

- (A) Radioiodine
- (B) Dietary changes
- (C) Antiretrovirals
- (D) Antibiotics
- (E) Corticosteroids

**The answer is D: Antibiotics.** Chronic diarrhea is defined as a decrease in stool consistency that lasts longer than 4 weeks. There are many causes of chronic diarrhea, and the diagnosis often requires an extensive workup. Important diagnostic categories to consider are infections, osmotic diarrhea (with an increased stool osmotic gap, such as lactose intolerance), secretory diarrhea (e.g., hormones, laxative abuse), chronic inflammation (e.g., inflammatory bowel disease, ischemic colitis), functional diarrhea (decreased motility, such as irritable bowel syndrome), and malabsorption (e.g., pancreatic disease, celiac disease).

This patient has Whipple disease, a rare cause of chronic diarrhea that is due to infection with *Tropheryma whippeli*. Though this bacterial species can infect a wide variety of patients, the majority are middle-aged Caucasians, with a large percentage being farmers (or at least having exposure to soil or animals). Four features that suggest the diagnosis are chronic diarrhea, abdominal pain, weight loss, and migratory arthralgias; however, the disease may present without any GI symptoms and can alternatively present with CNS disease or endocarditis. The diagnosis is confirmed with biopsy showing an abundance



of macrophages in the lamina propria with intracellular material that stains positive with PAS.

(A) Radioiodine would be an appropriate treatment for hyperthyroidism, which can also cause weight loss and diarrhea but is unlikely to cause migratory arthralgias. (B) Dietary changes would cure conditions such as lactose intolerance or celiac disease, but would play no role in this disease. (C) HIV is often a right answer on the examination, and chronic diarrhea is a common complaint in patients with HIV (for many reasons, including infection with *Cryptosporidium*, the use of antiretrovirals, etc.); however, the biopsy results confirm the diagnosis of Whipple disease. (E) Corticosteroids are the treatment of microscopic colitis, a cause of chronic diarrhea that will also have a normal appearance on colonoscopy. Biopsy will show normal architecture but many inflammatory cells, and staining with PAS would be negative.

32

A 51-year-old man with a history of poorly controlled diabetes mellitus presents to the Emergency Department with fever, headache, purulent nasal discharge, and decreased vision. The symptoms began in the morning and have rapidly progressed. The patient is now confused and lethargic. He is febrile and tachycardic, and physical examination reveals bilateral proptosis, perinasal swelling, and a large palatal eschar. His laboratory values are significant for a leukocyte count of  $19,000/\text{mm}^3$  and a glucose of 468 mg/dL. His urine dipstick is positive for protein, glucose, and ketones. A biopsy is taken and confirms the diagnosis.

What is the most important next step in management?

- (A) Vancomycin and piperacillin-tazobactam
- (B) IV fluids and insulin
- (C) Deferoxamine
- (D) Amphotericin B

**The answer is D: Amphotericin B.** Mucormycosis is a rapidly progressive infection caused most commonly by the fungi *Mucor*, *Rhizopus*, and *Rhizomucor*. While there are other presentations of mucormycosis (e.g., pulmonary and renal mucormycosis), the most common manifestation is infection of the nasal cavity that extends into the sinuses, orbits, and the brain and causes severe inflammation and necrosis. The main risk factor for this infection is immunosuppression, and a large proportion of patients are diabetic. It is common for diabetic patients with mucormycosis to have ketoacidosis. Though the prognosis is poor, rapid surgical debridement and antifungal therapy with amphotericin B provides the best outcomes. (A) Broad spectrum antibiotic regimens are not effective against these fungal species. (B) IV fluids and insulin will also be given to this patient, and managing the patient's hyperglycemia and ketoacidosis will improve the outcome. However, the most important lifesaving therapy is surgery and antifungals, and this should not be delayed. (C) Deferoxamine is used as an iron chelator and actually *increases* the risk of mucormycosis.

33

An 83-year-old man is transferred to the hospital from his nursing home due to hypotension and confusion. He was previously well until yesterday morning, when the nursing staff observed that he seemed lethargic and spent the day in bed. Later that night, the staff tried to communicate with him but he was not oriented to place or time. His medical history is significant for hypertension, COPD, paroxysmal atrial fibrillation, and urinary incontinence requiring a urethral catheter. He is compliant with medications, has no recent medication changes, and has no sick contacts. On examination, his temperature is 35.4°C, his blood pressure is 68/44 mmHg, his heart rate is 88 beats per minute, and his respiratory rate is 18 breaths per minute. He is lethargic with flat neck veins; his cardiac examination is normal. His lungs are clear to auscultation, and there is no significant abdominal tenderness. His neurologic examination is normal, and his extremities are warm and well perfused. His laboratory values are significant for a leukocyte count of 13,500/mm<sup>3</sup> and a serum lactate of 3.9 mmol/L (normal range 0.6 to 2.3 mmol/L). A urinalysis shows significant pyuria. A chest x-ray shows hyperinflated lungs but no focal opacities.

Which of the following is the most appropriate next step in management?

- (A) Rapid administration of normal saline
- (B) Heavy diuresis with IV furosemide
- (C) Administration of empiric ceftriaxone and piperacillin-tazobactam
- (D) Administration of activated protein C
- (E) Administration of hydrocortisone
- (F) Administration of norepinephrine

**The answer is A: Rapid administration of normal saline.** This patient meets SIRS criteria with a likely source of infection: urinary tract infection (UTI), which is suggested by pyuria. In addition, he is hypotensive with an elevated lactate, which indicates that this patient has severe sepsis. Although the management of sepsis is not tested in detail, it is useful to know some of the general principles. First, access should be obtained with two large-bore IVs and normal saline should be administered immediately (note that this would be harmful if the cause of shock is heart failure, so it is first important to diagnose the correct type of shock). (F) If the patient's blood pressure is not responding to heavy IV fluids (as per early goal-directed therapy targeting a mean arterial pressure  $\geq 65$  mmHg), then vasopressors can be given. Source control is also important; if there is an obvious source of infection, such as this patient's urinary catheter, it should be removed immediately. (C) Empiric antibiotics should be started immediately, but preferably after two sets of blood cultures are obtained from separate venipuncture sites. Antibiotics should have broad coverage and be directed at the potential source of infection if possible. The combination of ceftriaxone and piperacillin-tazobactam

is not a good regimen, since both are  $\beta$ -lactams; in addition, MRSA is a common cause of sepsis and is not being covered with this regimen. (D, E) Activated protein C is no longer recommended for the treatment of sepsis, and the benefit of hydrocortisone is unclear (it may be tried with hypotension refractory to IV fluids and vasopressors). (B) This patient is not in heart failure, as indicated by the low jugular venous pressure, and so diuresis with furosemide could be disastrous.

34

A 32-year-old woman suddenly develops abdominal pain and diarrhea. The abdominal pain is periumbilical and crampy, and she has had about 10 episodes of diarrhea per day over the past 3 days. She has no past medical or surgical history. She reports no sick contacts or recent travel, and no animal exposures. About 3 days ago she ate chicken at a barbecue that she thought might have been undercooked, but denies any other unusual food exposures. Stool studies are positive for fecal WBCs and fecal occult blood; stool culture eventually grows out *Campylobacter jejuni*. She is treated with IV fluids and ciprofloxacin and is discharged home. About 2 weeks later, she develops weakness and absent deep tendon reflexes involving the lower extremities bilaterally.

All of the following are also triggers for this complication, EXCEPT.

- (A) *Chlamydia trachomatis* infection
- (B) Influenza-like illness
- (C) HIV
- (D) Vaccination

**The answer is A: *Chlamydia trachomatis* infection.** This is a typical presentation of *Campylobacter* infection, which causes an acute inflammatory diarrhea indicated by the positive fecal leukocytes and RBCs. Common exposures include undercooked chicken and unpasteurized milk, and puppies and kittens can carry the organism. *Campylobacter* infection is a well-described trigger for Guillain-Barré syndrome (GBS), which presents as an acute ascending motor neuropathy (although there are variants, such as the Miller Fisher syndrome that presents as a descending neuropathy that may involve the cranial nerves). The pathogenesis is likely the result of antibody formation through the mechanism of molecular mimicry. (B, C, D) Preceding upper respiratory tract infections, HIV, and some vaccinations (influenza, meningococcal, etc.) are also associated with GBS. *Chlamydia trachomatis* infection is associated with reactive arthritis, not GBS. (Of note, *Campylobacter* and other enteric bacteria such as *Salmonella*, *Shigella*, *Yersinia*, and *C. difficile* can also cause reactive arthritis weeks after a diarrheal illness.)

35

A 32-year-old woman presents with recurrent dysuria. She was diagnosed with a UTI twice in the past 3 months, and was treated with 3 days of ciprofloxacin each time. The symptoms went away with treatment;

however, they continue to recur. She currently complains of dysuria, frequency, and urgency similar to her previous episodes. Her previous urine culture results have all grown out *Proteus mirabilis*. A urine dipstick is positive for leukocyte esterase, nitrites, and blood; the urine pH is 8.1.

What is the most appropriate management of this patient?

- (A) Oral ciprofloxacin for 3 days
- (B) IV ceftriaxone for 7 days
- (C) Oral ciprofloxacin for 3 days, with refills so the patient may self-treat if symptoms recur
- (D) CT scan of the abdomen and pelvis
- (E) Reassurance

**The answer is D: CT scan of the abdomen and pelvis.** UTIs are a common problem, and this patient presents with recurrent symptoms (dysuria, frequency, urgency) and signs (positive urine dipstick and culture) of cystitis. “Uncomplicated” cystitis refers to nonpregnant women without any structural or neurologic abnormalities and not immunosuppressed. The most frequent pathogens that cause uncomplicated UTIs are *E. coli*, *Proteus*, *Klebsiella*, and *S. saprophyticus* (especially in young, sexually active women). The fact that this patient has recurrent cystitis by *Proteus* raises the concern that there is a renal stone that might be acting as a nidus for recurrent infections. *Proteus* alkalinizes the urine with the enzyme urease and causes struvite stone formation (magnesium ammonium phosphate). Many of these stones are asymptomatic, but should be removed to prevent renal damage and recurrent infections.

(A, B) Oral ciprofloxacin and IV ceftriaxone are used to treat cystitis and pyelonephritis, respectively. (C) Self-treatment is an option for patients with recurrent cystitis; however, a urinary stone must first be ruled out in this patient given the frequency of *Proteus* infections. Risk factors for recurrent cystitis include the use of spermicide, frequent sexual intercourse, and any cause of decreased bladder emptying. (E) Reassurance is only appropriate in asymptomatic bacteriuria in nonpregnant patients.



36 A 27-year-old woman presents to the Emergency Department with confusion and a high fever. She was at a party earlier in the week and admits to heavy drinking and IV drug use; since then, she has developed fever, chills, fatigue, and shortness of breath. She has no previous medical or surgical history. Her temperature is 39.2°C, blood pressure is 110/74 mmHg, heart rate is 96 beats per minute, respiratory rate is 24 breaths per minute, and oxygen saturation is 97% on room air. On examination, she has elevated jugular venous pressure and a holosystolic murmur heard over the left lower sternal border. A chest x-ray shows several round opacities in bilateral lung fields.

Which of the following represents the correct order in the workup of this patient?

- (A) Start vancomycin, then send for immediate valvular surgery
- (B) Start vancomycin, gentamicin, and cefepime, obtain blood cultures, then perform a transesophageal echocardiogram
- (C) Obtain blood cultures, start vancomycin, then perform a transthoracic echocardiogram
- (D) Obtain blood cultures, start ceftriaxone and gentamicin, then perform a transesophageal echocardiogram
- (E) Obtain blood cultures, perform a transthoracic echocardiogram, then await culture results to start antibiotics

**The answer is C: Obtain blood cultures, start vancomycin, then perform a transthoracic echocardiogram.** This patient has evidence of acute bacterial endocarditis, which she likely contracted as a result of IV drug use. The holosystolic murmur over the left lower sternal border with an elevated jugular venous pressure is consistent with tricuspid regurgitation. In general, right-sided valvular lesions are more common in IV drug users, and these vegetations can send septic emboli to the lungs and cause pulmonary symptoms. When infective endocarditis is suspected, three blood cultures from three different venipuncture sites should be collected immediately. Only after cultures are drawn should antibiotics be started. The majority of endocarditis in IV drug users is caused by *S. aureus*, and MRSA is a concern. (E) Patients without acute symptoms can forgo empiric antibiotics and await blood culture results to start definitive antibiotic therapy. However, this patient is symptomatic and therefore empiric antibiotic therapy with vancomycin is warranted. A TTE is typically performed before a TEE, since it is less invasive. However, the sensitivity is much lower than a TEE, and therefore a nondiagnostic result or a negative result should be followed up with a TEE if the clinical suspicion is high.

(A) This patient is hemodynamically stable with no history of a prosthetic valve or indicators of a complicated infection, and therefore surgery is not appropriate at this time. (B) Vancomycin, gentamicin, and cefepime is an appropriate antibiotic regimen for the treatment of symptomatic prosthetic valve endocarditis. In addition, antibiotics should be started *after* blood cultures are collected. (D) Ceftriaxone and gentamicin can be used for empiric treatment of subacute bacterial endocarditis, which presents with a more indolent course than acute bacterial endocarditis.



- 37** A 62-year-old man is hospitalized to receive chemotherapy. His treatment course is complicated by neutropenia (serum neutrophil count  $<500/\mu\text{L}$ ), and he develops a temperature of  $38.6^{\circ}\text{C}$ . On examination, his IV lines are clean without surrounding erythema, his lungs are clear to auscultation, and he has no other obvious sources of infection.

What should be done next in the management of this patient?

- (A) Take blood cultures and treat with antibiotics if positive
- (B) Start vancomycin
- (C) Start cefepime
- (D) Continue treatment and observe

**The answer is C: Start cefepime.** Febrile neutropenia is a medical emergency, and patients are at high risk of developing a wide range of severe and rapidly progressive infections (gram-positive bacteria such as staph and strep, gram-negative bacteria such as *Pseudomonas* and *E. coli*, viruses such as HSV and CMV, fungi such as *Candida* and *Aspergillus*, etc.). Neutropenic fever is defined by an absolute neutrophil count  $<500/\mu\text{L}$  (indicates severe neutropenia) with a single temperature  $>38.3^\circ\text{C}$  or a temperature  $>38.0^\circ\text{C}$  for at least 1 hour. Empiric antibiotics should be started immediately after blood cultures are drawn. Because *Pseudomonas* is a common cause of serious infections in neutropenic patients (though gram-positive bacteria are now the most common cause), the chosen antibiotic(s) should have good *Pseudomonas* coverage. Cefepime is an appropriate option since it also has good gram-positive coverage.

(A) Blood cultures should be drawn, but empiric antibiotics should also be given right away. (B) Vancomycin for MRSA coverage does not need to be started empirically unless there are specific concerns for MRSA infection. (D) Because febrile neutropenia can progress rapidly and be life-threatening, observation is not appropriate.



A 28-year-old woman presents with fever, sore throat, and lymphadenopathy. A further history reveals that she has had unprotected sex with multiple partners. A screening HIV test is positive, which is confirmed with a Western blot. The woman has no other medical problems, does not use any illicit drugs, and desires to get pregnant. The decision is made to begin treatment with antiretrovirals.

Which of the following is an appropriate regimen for this patient?

- (A) Darunavir, fosamprenavir, and enfuvirtide
- (B) Emtricitabine, rilpivirine, and tenofovir
- (C) Didanosine, tenofovir, and tipranavir
- (D) Tenofovir, emtricitabine, and efavirenz

**The answer is B: Emtricitabine, rilpivirine, and tenofovir.** Because there is disagreement about when to start antiretroviral therapy in HIV patients, this topic is less likely to show up on the examination. Although antiretrovirals should be considered for every patient, strong indications include a CD4 count  $<500/\text{mm}^3$ , pregnancy, an AIDS-defining illness, and the presence of other significant comorbidities. Treatment-naïve HIV patients should generally start treatment with two NRTIs and either an NNRTI, a protease inhibitor (with or without ritonavir), or an integrase inhibitor. The only answer choice that

satisfies this rule and takes into account the possibility of future pregnancy is **B. (D)** This combination is normally a good option for initiating treatment, but efavirenz is teratogenic. **(A)** This is a combination of two protease inhibitors and an agent that is not approved for treatment-naïve patients (enfuvirtide), and so this is a poor option. **(C)** The combination of tenofovir and didanosine has a high failure rate.

39

A 33-year-old woman receives oral antibiotics to treat a mild UTI. She goes on a run, and feels a “pop” above her heel that is associated with severe pain. She has pain and difficulty with plantarflexion of the affected foot.

Which of the following antibiotics is most likely responsible?

- (A)** Trimethoprim-sulfamethoxazole
- (B)** Metronidazole
- (C)** Tobramycin
- (D)** Ciprofloxacin
- (E)** Azithromycin

**The answer is D: Ciprofloxacin.** One reported adverse reaction of fluoroquinolone antibiotics is tendinopathy, and the Achilles tendon is most often affected. Fluoroquinolones can also cause GI upset, dizziness, rash, and a prolonged QT interval. **(A)** Trimethoprim-sulfamethoxazole may cause Stevens–Johnson syndrome, leukopenia, hyperkalemia, hypoglycemia, and hepatitis. The incidence of adverse reactions is much higher in HIV patients. **(B)** Metronidazole can cause a disulfiram-like reaction with alcohol. **(C)** Tobramycin and other aminoglycosides may cause renal failure and ototoxicity. **(E)** Azithromycin and other macrolides can cause a prolonged QT interval and hepatitis.

40

A 68-year-old woman with a history of hypertension and poorly controlled diabetes presents for further management of her foot ulcer. She has had several weeks of wound care, but the ulcer is not healing. She has had ulcers previously and has been diagnosed with peripheral neuropathy and peripheral arterial disease. On examination, there is a 3-cm ulcer on the left foot with surrounding erythema and purulence. Her laboratory values show an ESR of 102 mm/h. An x-ray is taken of the foot, which is normal.

Which of the following would be most helpful in making the diagnosis?

- (A)** Wound culture
- (B)** MRI of the foot
- (C)** Bone biopsy
- (D)** No further diagnostic workup is necessary; continue wound care and topical antibiotics

**The answer is B: MRI of the foot.** Large diabetic foot ulcers, an ESR  $>70$  mm/h, and failure to respond to wound care after several weeks suggest the possibility of osteomyelitis. Although plain radiographs can be used to make the diagnosis, they are not very sensitive and are often indeterminate or normal. The next step in diagnosis is performing an MRI, which is a much more sensitive test. (A) Most diabetic foot ulcers are colonized with bacteria, and infections are often polymicrobial; thus, wound culture is of limited utility. Common organisms that cause diabetic foot infections include *S. aureus* (including MRSA), *S. epidermidis*, *S. pyogenes*, *Pseudomonas*, *Enterobacteriaceae*, and anaerobes. (C) Biopsy and culture of the bone can be helpful in making the diagnosis and guiding treatment; however, MRIs are less invasive and should be performed first. If a plain radiograph is normal, it is best to follow-up with MRI; if the results of MRI are nondiagnostic, and if the patient fails to respond to empiric antibiotics, then a bone biopsy should be performed. (D) Wound care and topical antibiotics are not effective in cases of osteomyelitis. Definitive antibiotic therapy is guided toward culture and sensitivity data when available; however, empiric therapy should be started early and chosen based on the extent of disease. An appropriate regimen would cover gram-positive cocci (including MRSA), aerobic gram-negative bacilli, and anaerobes. An example is clindamycin with ciprofloxacin.

41

A 63-year-old man presents to the physician complaining of fever and cough. One week ago, he developed fever, a nonproductive cough, and myalgias. He started to feel better after 3 days, but then the fever came back and his cough became productive of dark yellow sputum. He is now short of breath with any activity. His past medical history is negative for pulmonary disease, and he has never smoked tobacco. He has a fever of  $39^{\circ}\text{C}$  and is tachypneic. A chest x-ray shows pulmonary infiltrates.

Which of the following is likely to be seen on Gram stain of the expectorated sputum?

- (A) Gram-positive cocci in clusters
- (B) Gram-positive bacilli
- (C) Gram-positive cocci in chains
- (D) Gram-negative cocci
- (E) Gram-negative bacilli
- (F) No bacteria seen

**The answer is A: Gram-positive cocci in clusters.** *S. aureus* pneumonia is commonly seen in patients recovering from influenza. Notice that lancet-shaped gram-positive diplococcus was not an answer choice, since this is actually the most common organism to cause postinfluenza pneumonia (*S. aureus* is the second most common). Both young and old patients



recovering from influenza are at risk for secondary bacterial infection, since the primary infection and surrounding inflammation causes cellular damage leading to loss of cilia and other defense mechanisms. Therefore, if *S. aureus* pneumonia is suspected based on the history of a preceding viral infection, empiric antibiotics should include coverage of MRSA until more information is obtained from Gram stain and culture.

The following important organisms match the description on Gram stain: **(B)** *Clostridium* (“box-shaped”), *Listeria* (variable shapes), *Nocardia* (“branching”), *Corynebacterium* (“Chinese letters”); **(C)** *Streptococcus pyogenes* (group A strep), *Enterococcus*, *Peptostreptococcus*; **(D)** *Moraxella catarrhalis* (diplococcus), *Haemophilus influenzae* (coccobacillus); **(E)** *Pseudomonas*, *Klebsiella*, *E. coli*, *Enterobacter*, *Serratia marcescens*, *Acinetobacter* (pleomorphic); **(F)** Some organisms are not visualized by Gram stains (e.g., *Mycoplasma*, *Chlamydia*).

42

A 62-year-old man presents with fever, headache, and nuchal rigidity. His mental status is intact, and he has not experienced any seizures. He is admitted to the hospital with a presumptive diagnosis of meningitis, and a lumbar puncture is performed and shows slightly cloudy CSF without significant blood or xanthochromia. Screening blood laboratory values and CSF studies are pending.

What antibiotics should be started at this time?

- (A)** Ceftriaxone and vancomycin
- (B)** Acyclovir
- (C)** Ceftriaxone, vancomycin, and ampicillin
- (D)** Ceftriaxone, vancomycin, and dexamethasone
- (E)** Ceftazidime, vancomycin, ampicillin, and acyclovir

**The answer is C: Ceftriaxone, vancomycin, and ampicillin.** Since blood and CSF cultures may take days to provide the identity of the causative organism as well as information about antibiotic sensitivities, it is important to have an understanding of common organisms and the empiric antibiotics that will cover them. The most common cause of bacterial meningitis is *S. pneumoniae*, which is often resistant to penicillin. Therefore, empiric antibiotic regimens typically include ceftriaxone, which has activity against most strains of *S. pneumoniae*. However, there are strains of *S. pneumoniae* that are resistant to third-generation cephalosporins, and therefore vancomycin is added to the regimen to cover these resistant strains. **(A)** In children, alcoholics, and older patients (>50 years old), *Listeria* is a potential pathogen and therefore ampicillin should be added to the regimen.

**(B)** Acyclovir is used empirically in cases of suspected HSV encephalitis, which will often present with RBCs in the CSF and mental status changes. (Note: Xanthochromia refers to yellowish discoloration of the CSF caused by metabolized heme, which can be seen in subarachnoid hemorrhage.)

(D) Dexamethasone has shown a benefit in patients with meningitis due to *S. pneumoniae*; the greatest benefit is giving this to patients with a depressed mental status and with the first dose of empiric antibiotics (before culture data). This would be an appropriate answer choice if it included ampicillin in the regimen. (E) In patients who are immunosuppressed, a good regimen includes vancomycin, ceftazidime, ampicillin, and acyclovir.

Another point to consider is that antibiotic prophylaxis should be given to close contacts of patients with meningitis due to *N. meningitidis*. Options include rifampin, ciprofloxacin, or ceftriaxone. Rifampin is also the prophylactic antibiotic of choice for close contacts of *H. influenzae*.

43

A 36-year-old woman presents to her physician worried that she is pregnant. She is married and has been sexually active with her husband, and they normally use condoms for contraception. However, his condom broke during intercourse and she is now worried that she will become pregnant. She has urine studies performed, which show a negative pregnancy test and growth of *E. coli* from a clean-catch specimen. Two weeks later, she follows up for repeat testing, which give the same results. She denies any fevers, chills, flank pain, dysuria, hematuria, urgency, or frequency.

What should be done next in the management of this patient?

- (A) IV ceftriaxone
- (B) Oral ciprofloxacin
- (C) Measure serum human chorionic gonadotropin levels ( $\beta$ -hCG)
- (D) Reassurance

**The answer is D: Reassurance.** This patient has asymptomatic bacteriuria, defined as two clean-catch urine specimens that grow  $\geq 10^5$  colony forming units per mL. Only pregnant patients and those undergoing significant urologic procedures need to be treated with antibiotics. (A) This is a treatment option for inpatient management of pyelonephritis. (B) This is one of the standard treatments for cystitis, with other empiric options including nitrofurantoin and trimethoprim-sulfamethoxazole. (C) The urine pregnancy test reacts to urinary  $\beta$ -hCG, and serum levels do not need to be measured. Situations in which it is useful to measure serum  $\beta$ -hCG include ectopic pregnancy and gestational trophoblastic disease.

44

A 31-year-old woman presents to an obstetrician for prenatal care. She is 12 weeks pregnant based on her last menstrual period, and has been taking her prenatal vitamins during this time. She has been pregnant twice before, and both pregnancies resulted in miscarriages. Her medical history is significant for hypertension and a previous deep venous thrombosis. She takes no other medications and is allergic to penicillin

and cephalexin. As part of a routine workup, she is tested for syphilis and HIV. Serologic testing for HIV is negative, and her rapid plasma reagin (RPR) is reactive.

What is the most appropriate next step in management?

- (A) Testing for fluorescent treponemal antibody absorption (FTA-ABS) reactivity and screening for autoantibodies
- (B) Administer penicillin now
- (C) Administer doxycycline now
- (D) Undergo penicillin-desensitization, followed by treatment with penicillin immediately
- (E) Undergo penicillin-desensitization, followed by treatment with penicillin at delivery

**The answer is A: Testing for fluorescent treponemal antibody absorption (FTA-ABS) reactivity and screening for autoantibodies.**

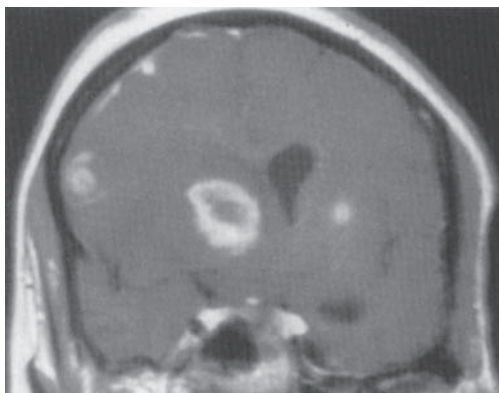
There is a high rate of both false positives and false negatives with both nontreponemal (e.g., RPR, VDRL) and treponemal tests (e.g., FTA-ABS) for syphilis. One commonly tested cause of a false-positive test is SLE, especially the antiphospholipid syndrome. This patient's history is concerning for the antiphospholipid syndrome given her history of multiple miscarriages and a thrombotic event. False-positive syphilis tests occur due to cross-reactivity with antiphospholipid antibodies (anticardiolipin, anti- $\beta_2$ -glycoprotein I, or lupus anticoagulant); a reactive nontreponemal test followed by a nonreactive treponemal test indicates a false-positive test. The patient should also be screened for SLE and antiphospholipid antibodies, given the suspicion for one of these diagnoses. (B, D, E) If this patient were to have syphilis, she should be desensitized to penicillin since she has a penicillin allergy and then treated immediately with penicillin, since this is the only therapy shown to be safe and effective during pregnancy. (C) In nonpregnant patients, other antibiotic options (e.g., doxycycline, azithromycin) are available for the treatment of syphilis; however, doxycycline is teratogenic.

An important cause of a false-negative syphilis test is the prozone reaction. This occurs in cases where there are high levels of serum antibodies (e.g., secondary syphilis) that interfere with agglutination. The specimen must be diluted for agglutination to occur and cause a positive result.

45

A 45-year-old woman with a history of HIV presents to the hospital with worsening confusion, headache, and fever. She has not been to her physician for follow-up in years, and has not been compliant with her medications. She has been hospitalized twice in the past year for pneumonia. Her last CD4 count measured 6 months ago was  $140/\text{mm}^3$ . She is admitted and found to be febrile to  $38.6^\circ\text{C}$ . She appears lethargic

and vomits several times. Her CD4 count is measured again during this hospitalization and is found to be  $76/\text{mm}^3$ . An MRI is performed, and the postcontrast T1-weighted image is shown in *Figure 6-12*.



**Figure 6-12**

Which of the following could have prevented this from happening?

- (A) Azithromycin prophylaxis
- (B) Yearly cancer surveillance
- (C) Trimethoprim-sulfamethoxazole prophylaxis
- (D) Isoniazid and pyridoxine for 9 months
- (E) There is no available treatment

**The answer is C: Trimethoprim-sulfamethoxazole prophylaxis.** Encephalitis is the most common manifestation of *Toxoplasma gondii*, and this organism may reactivate to form CNS abscesses when the CD4 count drops below  $100/\text{mm}^3$ . Suspect this diagnosis in HIV patients who are not taking prophylactic antibiotics and who have multiple ring-enhancing lesions on brain imaging. The acute treatment is pyrimethamine-sulfadiazine, and patients should receive trimethoprim-sulfamethoxazole prophylaxis until they have sufficient immune reconstitution on antiretroviral medications. Other important cutoffs to remember for antibiotic prophylaxis of opportunistic infections are trimethoprim-sulfamethoxazole for PCP prevention when the CD4 count is  $<200/\text{mm}^3$ , and azithromycin for mycobacterium avium complex (MAC) prevention when the CD4 count is  $<50/\text{mm}^3$ . If the CD4 count rises above these thresholds for  $>3$  to 6 months after antiretrovirals are started, antibiotic prophylaxis can be stopped.

(A) This patient's CD4 count is  $>50/\text{mm}^3$ , so azithromycin should not be started prophylactically. (B) HIV patients are at an increased risk of multiple cancers, including CNS lymphoma. As opposed to multiple ring-enhancing

lesions on brain imaging with toxoplasmosis, CNS lymphoma will typically present as a solitary lesion that may ring-enhance, although whole tumor enhancement is more common. Also look for a positive PCR test for EBV in a CSF sample. (E) Another important item on the differential diagnosis is progressive multifocal leukoencephalopathy (PML) due to polyomavirus JC (JC virus), which presents with multiple lesions that do not ring-enhance. It has a very poor prognosis and there is no treatment or specific preventive strategies other than antiretrovirals. (D) This is the treatment for latent TB, which may cause meningitis. Patients with HIV should be screened for latent TB, but there is no prophylactic treatment that is currently recommended to prevent TB infection.

46

A 40-year-old man with a history of HIV infection presents to his physician due to the development of several skin lesions. The lesions erupted over the past few days, and are associated with fevers, chills, and a headache. He had no other medical problems and admits to being inconsistent in taking his antiretroviral medications. He works at a pet adoption center, has not recently traveled, and has no known sick contacts. On examination, there are several violaceous papular and nodular lesions that vary in appearance on the patient's abdomen.

Which of the following is most likely responsible for these lesions?

- (A) *Mycobacterium avium* complex
- (B) Human herpesvirus-8 (HHV-8)
- (C) Human T-lymphotropic virus-1 (HTLV-1)
- (D) *Bartonella henselae*
- (E) Human papillomavirus (HPV)

**The answer is D: *Bartonella henselae*.** Both Kaposi sarcoma (due to HHV-8) and bacillary angiomatosis (due to *Bartonella henselae*) affect AIDS patients and are in the differential diagnosis of cutaneous vascular proliferations. A skin biopsy is often necessary to differentiate the two conditions, and both can progress from localized skin lesions to widespread lesions with visceral involvement. When systemic symptoms such as fevers, chills, anorexia, and headache are present, the diagnosis of bacillary angiomatosis should be considered. Exposure to cats is a risk factor, and the infection responds to treatment with doxycycline or erythromycin. (B) Kaposi sarcoma is in the differential, but is less likely to have systemic symptoms. Of note, Kaposi sarcoma does not only occur in AIDS patients, but may affect solid organ transplant recipients, older men from the Mediterranean region (classic form), and those in Africa (endemic form). Treatment is with intralesional chemotherapy or systemic chemotherapy (doxorubicin) if the lesions are widespread or visceral.

(A) MAC occurs due to infection with *M. avium* or *M. intracellulare* and typically occurs in patients with a CD4 count  $<50/\text{mm}^3$ . MAC infection may manifest as localized disease (focal lymphadenitis) or as disseminated disease

(fever, chills, night sweats, diarrhea, abdominal pain), but would not present with vascular skin lesions like the patient in this vignette. (C) HTLV-1 is associated with adult T-cell leukemia/lymphoma, which can have cutaneous manifestations but the lesions are typically patches, plaques, or nodules, and are not vascular like the lesions in this patient. (E) HPV can cause cervical or anal cancer in AIDS patients.

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**47** A 24-year-old medical student experiences an accidental needle stick from a patient known to have HIV.

Which of the following is the most appropriate management?

- (A) Tenofovir, emtricitabine, and raltegravir
- (B) Tenofovir and emtricitabine
- (C) Abacavir
- (D) Reassurance

**The answer is A: Tenofovir, emtricitabine, and raltegravir.** The risk of acquiring HIV from a needle stick is 0.3%, and the risk from mucosal contact is 0.09%. Even though the risk is low, the risk can be eliminated with postexposure prophylaxis (PEP). Currently, a three-drug regimen is recommended, and the combination of tenofovir-emtricitabine (individually or as a combination pill) and raltegravir has a low risk of adverse effects. (B) The use of tenofovir-emtricitabine alone is thought to be less effective than the three-drug regimen. (C) Abacavir has a high rate of life-threatening hypersensitivity reactions, so the risk would outweigh the benefit. (D) Although the patient can refuse PEP if he desires, reassurance would not be appropriate since there is a small chance that he may acquire HIV.

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**48** A 38-year-old man presents to his physician complaining of fatigue, weight loss, cough, and shortness of breath. The symptoms have been present for 2 weeks now, and he has lost 4 kg over this time. He also complains of waking up in the middle of the night drenched with sweat. The cough is productive of yellow sputum and occasionally small amounts of blood. His medical history is significant for hypertension, for which he takes chlorthalidone, and he has a 12 pack-year smoking history. His temperature is 38.3°C, blood pressure is 138/88 mmHg, heart rate is 96 beats per minute, and respiratory rate is 24 breaths per minute. On examination, he has a normal S1 and S2 with no murmurs or gallops on auscultation. There is dullness to percussion over the right lower portion of his anterior chest, with decreased breath sounds over this area. A chest x-ray shows consolidation of the right middle lobe, and the right heart border is obscured. He is treated with antibiotics and is discharged. The patient follows up in clinic a couple of weeks later, and his laboratory values reveal elevated liver enzymes and uric acid.

Which of the following agents could cause both of these findings?

- (A) Ceftriaxone
- (B) Vancomycin
- (C) Ethambutol
- (D) Isoniazid
- (E) Rifampin
- (F) Trimethoprim-sulfamethoxazole
- (G) Pyrazinamide
- (H) Furosemide

**The answer is G: Pyrazinamide.** This patient has primary TB, which presents with lobar consolidation typically of the lower lung segments (as opposed to reactivation of latent TB, which presents as an apical opacity; both primary and reactivation TB may have cavitation). It is important to know the treatment of active TB as well as the adverse effects of these medications. The treatment of active TB is “RIPE” therapy and can be remembered with the additional mnemonic of “4 for 2 and 2 for 4”: Rifampin, Isoniazid, Pyrazinamide, and Ethambutol for 2 months, then Rifampin and Isoniazid for 4 months. (Note: If drug-resistant TB is suspected, testing should be performed prior to initiating treatment to choose the most appropriate regimen.)

Toxicities of pyrazinamide include hepatitis, hyperuricemia, and a maculopapular rash. (D) Isoniazid also causes hepatitis, but it does not cause hyperuricemia. Another common adverse effect of isoniazid is peripheral neuropathy, which is why vitamin B<sub>6</sub> is given with isoniazid. One other high-yield toxicity is drug-induced lupus; other high-yield drugs that can cause this are hydralazine, procainamide, infliximab, and methyldopa. (E) Rifampin causes orange discoloration of body fluids, hepatitis, and has many drug–drug interactions (induces many enzymes of the cytochrome P450 family). (C) Ethambutol causes optic neuritis. (A, B, F, H) None of these drugs are used in the treatment of TB. Furosemide and other diuretics can cause hyperuricemia but would not have been given to this patient.

49

A 42-year-old man who recently immigrated to the United States from Turkey presents with lower urinary tract symptoms. He reports that 4 months ago he had a localized rash on his trunk after swimming in a lake. Within the past few weeks, he has developed urinary urgency, frequency, and pain with urination. He has no history of kidney stones, UTIs, or congenital urinary tract abnormalities. He is afebrile with a normal physical examination. His laboratory values are significant for a hemoglobin of 11.1 g/dL, and a serum leukocyte differential shows eosinophilia. Microscopic analysis of the urine reveals numerous RBCs and parasite eggs.

If left untreated, which of the following is this patient at risk of developing?

- (A) Bladder cancer
- (B) Portal hypertension
- (C) Severe hemolytic anemia
- (D) Asthma

**The answer is A: Bladder cancer.** *Schistosoma* species are parasites that are acquired through contact with fresh water. Many infections present initially as “swimmer’s itch,” which is a localized hypersensitivity reaction at the site where larvae enter through the skin. Once they enter the skin, they travel through the bloodstream to reach the liver and mature. Different species travel from the portal system to different areas of the body, causing variable disease manifestations. *S. mansoni* and *S. japonicum* produce disease of the liver and intestines, whereas *S. haematobium* produces disease of the urinary tract. There is an increased risk of squamous cell carcinoma of the bladder in patients with chronic infection due to *S. haematobium*.

(B) Other *Schistosoma* species that affect the liver and portal vein can cause portal hypertension. (C) Schistosomiasis is not associated with hemolytic anemia. This patient likely is anemic from blood loss in the urine. (D) Schistosomiasis can produce pulmonary hypertension by damaging the pulmonary vasculature; however, it will not cause airway disease. Airway disease such as asthma may be seen in parasite infections that involve the lungs as part of their lifecycle (e.g., *Strongyloides stercoralis*).



A 32-year-old man comes to the physician complaining of fever, shortness of breath, and a productive cough that has developed slowly over the past week. He has no other medical history and does not take any medications. His temperature is 38.5°C, blood pressure is 122/78 mmHg, heart rate is 68 beats per minute, respiratory rate is 18 breaths per minute, and oxygen saturation is 98% on room air. There are decreased breath sounds and dullness to percussion over the right lung base. The rest of the physical examination, including cardiac auscultation, is normal. A chest x-ray confirms consolidation of the right lower lobe.

What is the most appropriate course of action for this patient?

- (A) Outpatient treatment with azithromycin
- (B) Perform diagnostic blood and sputum tests, then treat as an outpatient with antibiotics based on the culture and sensitivities
- (C) Admit the patient and treat with levofloxacin
- (D) Admit the patient and treat with ceftriaxone and clindamycin

**The answer is A: Outpatient treatment with azithromycin.** This patient has typical symptoms of pneumonia (fever, productive cough, dyspnea), and



the diagnosis is confirmed by chest x-ray. Because this patient is young and healthy with no comorbidities, he can be treated for CAP as an outpatient with a macrolide antibiotic. Atypical causes of pneumonia (*Mycoplasma*, *Chlamydia*, viruses) are common in this age group; however, the specific pathogen cannot be reliably determined based on the symptoms/signs or chest x-ray. **(B)** If the decision is made to treat the patient as an outpatient, it is unnecessary to order blood and sputum cultures since empiric antibiotic treatment is almost always successful. An exception to this is macrolide-resistant *S. pneumoniae*, which should be considered in patients from a high resistance area or in patients who took a macrolide antibiotic in the last few months. Even if blood and sputum cultures are sent, empiric antibiotics should be started immediately and then changed if necessary based on the culture data. **(C, D)** Deciding whether or not to admit a patient is based on many factors, and tools such as the pneumonia severity index, CURB-65, and SMART-COP (to determine the need for intensive care) can help in making this decision. Though this is low yield for the shelf examination, it might be helpful to know CURB-65: confusion, uremia/BUN  $\geq 20$  mg/dL, respirations  $\geq 30$  breaths per minute, blood pressure  $< 90/60$  mmHg, age  $\geq 65$  years. Scores of 0 to 1 can be treated as an outpatient, a score of 2 should be treated as an inpatient, and scores  $\geq 3$  may benefit from intensive care.



**51** A 52-year-old woman with a history of diabetes mellitus and hypertension presents to the Emergency Department with fevers, chills, and abdominal pain. The symptoms began about 1 week ago and have been getting worse. The abdominal pain is associated with nausea and vomiting, and she has not been able to eat. On examination, her temperature is  $38.8^{\circ}\text{C}$ , blood pressure is 104/68 mmHg, heart rate is 94 beats per minute, and respiratory rate is 16 breaths per minute. Her abdominal examination shows right-sided pain to deep palpation, and she has severe right-sided costovertebral angle tenderness. Her laboratory values are shown below.

|                                |                                                    |
|--------------------------------|----------------------------------------------------|
| Leukocyte count                | 14,200/mm <sup>3</sup>                             |
| Bicarbonate                    | 21 mEq/L                                           |
| Creatinine                     | 1.1 mg/dL                                          |
| Glucose                        | 184 mg/dL                                          |
| Erythrocyte sedimentation rate | 54 mm/h                                            |
| Urinalysis                     | Significant WBCs, WBC casts, protein, and bacteria |

A urine culture returns positive for *E. coli* that is sensitive to ceftriaxone and ciprofloxacin. She is treated with IV ceftriaxone, but after 3 days of treatment she continues to be febrile.

What is the most appropriate next step in management?

- (A) Renal biopsy
- (B) CT scan with contrast
- (C) Continue the current antibiotic
- (D) Stop ceftriaxone and start ciprofloxacin

**The answer is B: CT scan with contrast.** This patient has pyelonephritis that likely progressed to a renal or perinephric abscess, which is indicated by the persistent fever. Patients with this complication will present with symptoms typical of pyelonephritis (fevers, chills, flank pain, abdominal pain, anorexia, nausea/vomiting), but will continue to be febrile despite treatment with appropriate antibiotics. Most cases of renal/perinephric abscesses are caused by urologic pathogens (e.g., *E. coli* and other enteric gram-negative bacilli); however, *S. aureus* is also common and arrives at the kidneys by hematogenous spread. The best diagnostic test is a CT scan of the abdomen with contrast, although a renal ultrasound can also identify many renal/perinephric abscesses. If the abscess is small, it can be observed with antibiotics alone; if the patient does not respond to antibiotics, or if the abscess is large, both antibiotics and drainage are necessary. Antibiotic therapy should always be based on culture and sensitivity data when available; however, empiric therapy for renal/perinephric abscesses is the same as for pyelonephritis. Options include a fluoroquinolone, ceftriaxone, ampicillin-sulbactam, an aminoglycoside, or anti-staphylococcal antibiotics if *S. aureus* is suspected.

(A) WBC casts do not necessarily indicate acute interstitial nephritis or glomerulonephritis; they may also indicate an upper UTI such as pyelonephritis. Therefore, a renal biopsy is not the next step. (C) Failure to defervesce after treatment with antibiotics raises the concern for a complication of pyelonephritis, such as a renal or perinephric abscess, and therefore further diagnostic workup should be pursued. (D) The organism is sensitive to both antibiotics, so there is no benefit of changing antibiotics.

52

An 83-year-old woman is hospitalized after an ischemic stroke. On day 2 of her hospitalization, she develops dyspnea. Her vitals show a temperature of 37.8°C, blood pressure of 146/90 mmHg, heart rate of 102 beats per minute, respiratory rate of 26 breaths per minute, and oxygen saturation of 89% on room air. There are diffuse bilateral rales on pulmonary auscultation. She is placed on supplemental oxygen, and a chest x-ray is ordered immediately, which shows bilateral infiltrates.

What is the most likely diagnosis?

- (A) Cheyne–Stokes respiration
- (B) Aspiration pneumonia
- (C) Airway obstruction
- (D) Chemical pneumonitis

**The answer is D: Chemical pneumonitis.** Patients are at an increased risk of aspiration with the following conditions: neurologic disorders (e.g., stroke), depressed consciousness (e.g., anesthesia), dysfunctions in swallowing or the normal defense barrier (e.g., achalasia, nasogastric tube), supine positioning, and many others. The diagnosis most consistent with the immediate development of dyspnea and hypoxemia is chemical pneumonitis, which occurs as a result of direct airway damage from gastric acid. The chest x-ray will show changes within hours of the aspiration event. Although most cases resolve shortly in a few days, it is not a benign diagnosis; it may progress to ARDS, and it may be fatal, especially in the critically ill. Therapy involves immediate tracheal suctioning and mechanical ventilation if necessary.

(A) Cheyne–Stokes respiration is an abnormal breathing pattern that may occur after a stroke; however, it would not cause hypoxemia with infiltrates on chest x-ray. (B) Many cases of aspiration will produce both chemical pneumonitis and pneumonia due to inhalation of oropharyngeal microbes; however, it takes days for the pneumonia to become symptomatic (and even longer if it is an anaerobic infection). Many physicians choose to place the patient on empiric antibiotics and discontinue them if the patient's chest x-ray is clear after 2 to 3 days. (C) An airway obstruction may occur after an aspiration event due to aspiration of particulate matter from the stomach. Without chemical pneumonitis, it would not produce chest x-ray infiltrates.

53

A 30-year-old man presents to his physician with a rash on his left leg. He reports that the rash started as a bug bite and is spreading. He denies any fever, chills, or malaise. His medical history is significant for type 1 diabetes mellitus, and his only medication is insulin. On examination of the left leg, there is a 4-cm area of erythema, swelling, and warmth with indistinct margins. There is no gross purulence.

What antibiotic should this patient receive?

- (A) Oral cephalexin
- (B) Oral dicloxacillin
- (C) Oral clindamycin
- (D) IV vancomycin

**The answer is C: Oral clindamycin.** This is a straightforward case of cellulitis, which is typically caused by *Streptococcus pyogenes* or *Staphylococcus aureus*. Patients with risk factors for MRSA (previous MRSA infection or

colonization, diabetes, HIV infection, recent hospitalization or antibiotics, IV drug use, etc.) or with gross purulence should receive an antibiotic that has MRSA coverage. Therapy is usually empiric (since skin cultures are rarely helpful) and is based on the clinical diagnosis and patient's risk factors. (A, B) Cephalexin and dicloxacillin are both appropriate antibiotics if MRSA was *not* a concern. (D) Although vancomycin has activity against MRSA, this patient has a localized infection without systemic symptoms and therefore can be treated as an outpatient with oral therapy.

For the sake of the shelf examination, there are a few other important soft tissue infections to know. Erysipelas is a more superficial infection of the dermis and is raised with distinct margins. The majority of cases are due to group A strep. Necrotizing fasciitis is caused by virulent strains of group A strep or MRSA and presents with a rapidly expanding lesion that is severely painful and may have crepitation. Treatment is with debridement and antibiotics to cover group A strep and MRSA (e.g., penicillin and clindamycin) unless the history and risk factors suggest an alternative pathogen. Gas gangrene is a life-threatening infection caused by *Clostridium perfringens* that spreads rapidly with necrosis and significant crepitus; treatment is with debridement and antibiotics (also penicillin and clindamycin). If the patient has a penetrating injury (e.g., diabetic patient that stepped on a nail that penetrated his shoe), consider *Pseudomonas*. In gardeners, consider *Sporothrix schenckii*, which spreads via lymphatics and causes ulcerating nodules. If there is exposure to saltwater, consider *Vibrio vulnificus*.

54

A 32-year-old man complains of fever, diarrhea, and abdominal pain. He has had intermittent fevers for the past month, with episodes of bloody diarrhea. The abdominal pain started 2 weeks ago, and since that time he has had fewer episodes of diarrhea. He denies any jaundice, pale stools, or IV drug use. The patient emigrated from Mexico 6 months ago, and has been living with his extended family in Arizona. On examination, there is hepatomegaly with tenderness to palpation over the liver. An abdominal ultrasound reveals a well-defined hypochoic mass.

What is the most likely pathogen responsible for this patient's symptoms?

- (A) *Entamoeba histolytica*
- (B) *Candida albicans*
- (C) *Escherichia coli*
- (D) *Diphyllobothrium latum*
- (E) *Klebsiella pneumoniae*
- (F) *Campylobacter jejuni*
- (G) *Salmonella typhi*
- (H) *Coccidioides immitis*

**The answer is A: *Entamoeba histolytica*.** Most infections due to the parasite *Entamoeba histolytica* are asymptomatic; however, this pathogen can cause invasive colitis presenting as dysentery. A common extraintestinal manifestation is liver abscess, which presents with fever and right upper quadrant abdominal pain. This patient recently emigrated from an endemic country and has suggestive symptoms of amebiasis complicated by a liver abscess. Diagnosis can be made with abdominal imaging and stool studies, and treatment is with both metronidazole and paromomycin (to eliminate luminal cysts). Amebic liver abscesses do not need to be drained and are usually treated successfully with medical therapy alone.

(B, E) Streptococcal species, *S. aureus*, *Candida*, and *Klebsiella* are all causes of liver abscess; however, the presentation of dysentery and recent immigration make amebiasis more likely. (C, F, G) *E. coli*, *Campylobacter*, and *Salmonella* can all cause invasive diarrhea but are not associated with liver abscesses. Of note, *Salmonella* can cause hepatosplenomegaly and also establish itself in a chronic carrier state in the gallbladder; however, this patient does not have other features of typhoid fever (“rose spot” rash, relative bradycardia, etc.). (D) *Diphyllobothrium latum* is a tapeworm that produces GI symptoms and can present with megaloblastic anemia (due to parasitic absorption of dietary vitamin B<sub>12</sub>). (H) *Coccidioides* is common in Arizona, but produces pulmonary symptoms; when it disseminates, it typically disseminates to the skin, meninges, or bone.

55

A 42-year-old man presents to his physician with fever, headache, and rash. Three days ago, he developed fever and a headache, which minimally improved with acetaminophen. This morning he noticed a rash on his wrists and ankles that spread to his torso. He has no past medical history and does not smoke. He recently returned from a camping trip in Virginia 1 week ago. On examination, he is febrile and there are scattered erythematous blanching macules over his arms, legs, and torso.

What should be done next in the management of this patient?

- (A) Administer doxycycline
- (B) Administer IV prednisone
- (C) Confirm the diagnosis with serology
- (D) Administer Penicillin G
- (E) Apply topical clobetasol

**The answer is A: Administer doxycycline.** Rocky Mountain spotted fever is caused by the bacterial species *Rickettsia rickettsii*, which is carried by the *Dermacentor variabilis* tick. Though infection may occur in many areas of the United States, it is most common in the Southeastern United States. The incubation period is typically around 1 week, after which nonspecific symptoms of fever, headache, and myalgias develop. A few days later, a maculopapular rash appears that starts on the wrists and ankles (also commonly affects the

palms and soles) and spreads to the trunk; it often evolves into a petechial rash. There is a high morbidity and mortality of this infection if it goes untreated, therefore doxycycline should be given empirically if the disease is suspected. (C) Testing for serum antibodies to *Rickettsia* will not be positive until about a week, which is too late; therefore, the diagnosis is usually confirmed with skin biopsy. (B) *Rickettsiae* infect the vascular endothelium, causing vascular damage and petechiae that may mimic a vasculitis; however, the recent travel and time course of the illness should lead the reader to suspect this infection and treat empirically with doxycycline. (D) Penicillin G is the treatment for syphilis, which can present with a maculopapular rash affecting the palms and soles (secondary syphilis). The patient's recent hiking trip in Virginia makes infection with *Rickettsia* more likely. (E) Topical clobetasol is a powerful corticosteroid that may be used in cases of contact dermatitis, which can vary in appearance but often cause a vesicular eruption without systemic symptoms.

(Note: Other important causes of a rash affecting the palms and soles include secondary syphilis and coxsackie virus; there are others, but these are the most commonly tested.)

## Hematology and Oncology

1

A 71-year-old man with a history of hypertension and hyperlipidemia presents with fatigue, diffuse joint pain, decreased appetite, and a weight loss of 5.44 kg (12 lb) over the last 4 months. Physical examination reveals splenomegaly. Laboratory studies reveal the following.

|                         |                         |
|-------------------------|-------------------------|
| Leukocyte count         | 29,000/mm <sup>3</sup>  |
| Hemoglobin              | 9.1 g/dL                |
| Mean corpuscular volume | 85 fL                   |
| Platelets               | 122,000/mm <sup>3</sup> |

Cytogenetic studies are performed and reveal an abnormal chromosome 22.

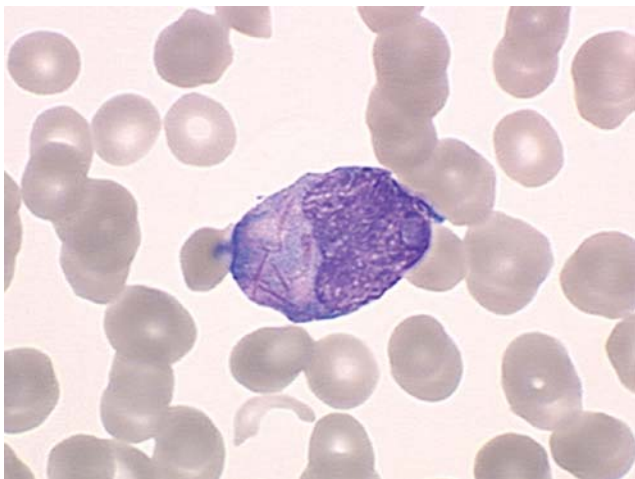
Which of the following is the appropriate treatment for this disease?

- (A) Methotrexate
- (B) All-trans-retinoic acid
- (C) Imatinib
- (D) Bone marrow transplant

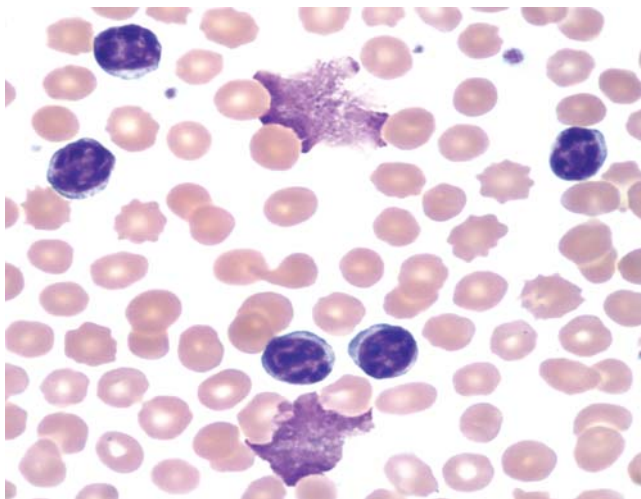
**The answer is C: Imatinib.** The patient in this question is presenting with leukocytosis, normocytic anemia, and thrombocytopenia. The abnormal chromosome 22 is likely the Philadelphia chromosome, a byproduct of the reciprocal translocation of chromosomes 9 and 22 that forms an abnormal *BCR-ABL* fusion gene, that ultimately results in aberrant tyrosine kinase activity. This abnormal fusion gene suggests the diagnosis of chronic myeloid leukemia (CML). Tyrosine kinase inhibitors, such as imatinib, are critical in the treatment of CML and act by binding to the ATP binding site of the *BCR-ABL* fusion gene so that it is unable to convert into its active form. (A) Methotrexate alters the metabolism of folic acid. Although it is commonly used in several other cancers and autoimmune conditions, it has no role in the treatment of CML. (B) All-trans-retinoic

acid is the carboxylic acid form of vitamin A and is used in acute promyelocytic leukemia, not in the treatment of CML. **(D)** Bone marrow transplant is a viable option for curing CML, but imatinib is the first-line treatment.

It is helpful to know peripheral blood smear findings for the different types of leukemia in preparation for the internal medicine shelf examination. In acute myeloid leukemia (AML), Auer rods are diagnostic (*Figure 7-1*). In chronic lymphocytic leukemia (CLL), smudge cells are diagnostic (*Figure 7-2*).



**Figure 7-1**



**Figure 7-2**



2

A 61-year-old woman with a history of diabetes mellitus, hypertension, and mechanical aortic valve replacement presents with fatigue and periodic palpitations when running. The patient does not endorse shortness of breath or chest pain. Her medications consist of warfarin, metformin, glyburide, lisinopril, and fish oil. On physical examination, she has conjunctival pallor, mechanical click during S2, and a soft systolic flow murmur. Fecal occult blood test is negative. Laboratory results reveal a hemoglobin of 10.1 g/dL, hematocrit of 29%, and a significantly elevated serum LDH. The peripheral blood smear is shown in Figure 7-3.

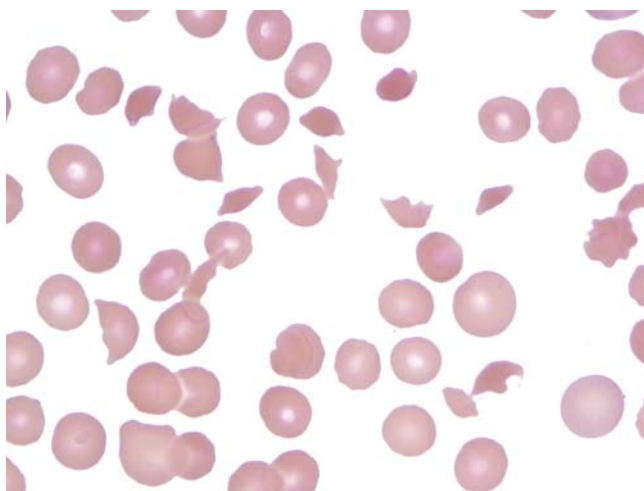


Figure 7-3

Which of the following is the underlying cause of this patient's condition?

- (A) Autoimmune hemolysis
- (B) Iron deficiency
- (C) Traumatic hemolysis
- (D) Bone marrow infiltration

**The answer is C: Traumatic hemolysis.** The patient in this question is presenting with anemia, elevated LDH, and schistocytes on peripheral blood smear. Increased LDH and schistocytes suggest increased red blood cell (RBC) *destruction* (i.e., hemolysis) as opposed to decreased RBC *production*. Traumatic hemolytic anemia is intravascular hemolysis caused by excessive shear or turbulence. Given that this patient has a mechanical

aortic valve, her anemia is most consistent with hemolysis secondary to RBC shearing on the valve. Other findings in the setting of hemolytic anemia include decreased haptoglobin and elevated indirect bilirubin. (A) Although autoimmune hemolytic anemia would also demonstrate elevated serum LDH, there will be *spherocytes*, rather than *schistocytes*, on peripheral blood smear. Furthermore, direct Coombs test will be positive. (B, D) Iron deficiency and bone marrow infiltration cause decreased RBC *production* rather than *destruction*.

**3** A 39-year-old man presents after tripping over his child's toy and subsequently falling down the stairs. The patient reports landing on his chest and now complains of pain over certain regions of his right chest wall. He endorses some mild pain on deep inspiration. The patient is otherwise healthy and denies alcohol or smoking. Physical examination demonstrates pain on palpation over the sternum. A chest x-ray is ordered which confirms two right rib fractures. The radiologist notes an incidental 2.25-cm coin-shaped lesion on the left upper lung. There is no associated adenopathy or atelectasis noted.

Which of the following is the most appropriate next step with respect to the solitary lung lesion?

- (A) CT scan of the chest
- (B) Lung biopsy
- (C) Review of an old chest x-ray
- (D) Reassurance

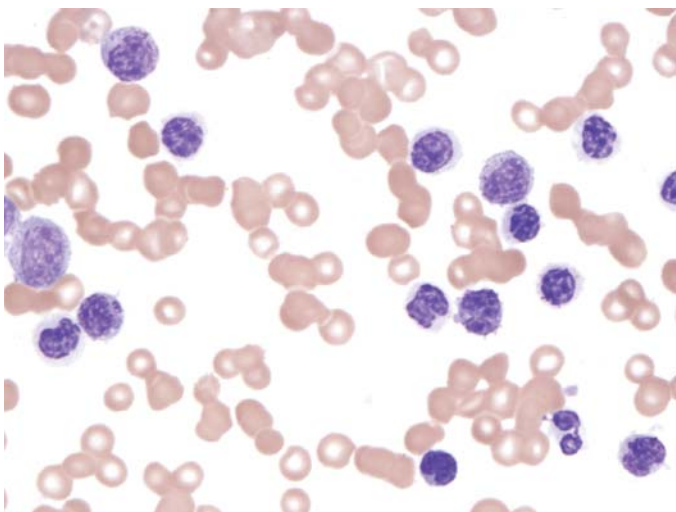
**The answer is C: Review of an old chest x-ray.** The patient in this question is presenting with rib fractures as well as the incidental finding of a solitary pulmonary nodule (SPN), which is defined as a discrete rounded opacity less than or equal to 3 cm in diameter. In addition, it must be completely surrounded by lung parenchyma and must not touch the hilum or mediastinum. Of note, lesions greater than 3 cm in diameter are considered malignancies until proven otherwise. The majority of SPNs are benign, especially if there are features such as calcifications and smooth edges. In low-risk patients (typically nonsmokers less than 40 years of age), the appropriate next step in management is to ask for an old chest x-ray (preferably within the last 12 months). If no change in the x-ray is noted, it is considered benign. It should then be followed every 3 months for the next year.

(A) If this patient were a smoker, a CT scan of the chest would be the best next step in workup after reviewing an old chest x-ray. (B) Typically after a CT scan of the chest is performed, a fine needle aspiration (FNA) is preferred to lung biopsy, but a biopsy can be considered if FNA does not generate significant results. (D) Although this patient is low risk, reassurance is not appropriate.

4

A 69-year-old woman presents with a 2-month history of worsening lower back pain, confusion, mild abdominal pain, weight loss, and constipation. She takes hydrochlorothiazide for hypertension and simvastatin for hypercholesterolemia. Her routine preventative screening measures were all up to date and within normal limits at her previous visit 5 months ago. Physical examination is unremarkable and fecal occult blood test is negative. Laboratory results and a peripheral blood smear (*Figure 7-4*) are shown below.

|                                |                         |
|--------------------------------|-------------------------|
| Leukocyte count                | 9,000/mm <sup>3</sup>   |
| Hemoglobin                     | 9.1 g/dL                |
| Platelets                      | 290,000/mm <sup>3</sup> |
| Blood urea nitrogen            | 32 mg/dL                |
| Creatinine                     | 2.1 mg/dL               |
| Erythrocyte sedimentation rate | 68 mm/h                 |
| Amylase                        | 67 U/L                  |



**Figure 7-4**

Which of the following additional findings do you expect with this patient's condition?

- (A) Mechanical obstruction
- (B) Electrolyte abnormality
- (C) Hormone level abnormality
- (D) Arterial blood gas abnormality

**The answer is B: Electrolyte abnormality.** The patient in this question is presenting with anemia, low back pain, increased erythrocyte sedimentation rate (ESR), and renal dysfunction, suggesting the diagnosis of multiple myeloma. The peripheral smear shows the rouleaux formation (stacked appearance of RBCs), which may also be seen in this condition. In addition, the patient is presenting with constipation and confusion, both symptoms of hypercalcemia ( $>10.2$  mg/dL), which is seen in about one-third of patients with multiple myeloma (however, this patient is also on a thiazide diuretic which may be worsening the hypercalcemia). The etiology of hypercalcemia in multiple myeloma is bone lysis from humoral factors released by the plasma cells. (A) Mechanical obstruction secondary to malignancy also can cause constipation, but the patient's signs and symptoms do not lend credence to colon cancer. (C, D) Hormone level and arterial blood gas abnormalities are typically not seen in multiple myeloma and are not associated with constipation.

5

A 9-year-old girl being treated with combination chemotherapy for acute lymphoblastic leukemia (ALL) is noted to have increased levels of blood urea nitrogen (BUN) and creatinine on day 4 of treatment. The patient is immediately started on intravenous normal saline. An ECG is ordered which demonstrates prolonged QT intervals. For confirmation of the diagnosis, several laboratory tests, including a complete metabolic profile, are ordered.

Which of the following laboratory abnormalities result from this patient's condition?

- (A) Decreased calcium, increased phosphate, decreased uric acid, decreased potassium
- (B) Decreased calcium, increased phosphate, increased uric acid, increased potassium
- (C) Decreased calcium, decreased phosphate, increased uric acid, increased potassium
- (D) Increased calcium, increased phosphate, increased potassium, increased uric acid

**The answer is B: Decreased calcium, increased phosphate, increased uric acid, increased potassium.** The patient in this question is demonstrating symptoms and signs of tumor lysis syndrome, a condition associated

with tumors with high cell turnovers. The tumors most frequently encountered with this condition include Burkitt lymphoma and the leukemias (particularly ALL). In order to confirm the diagnosis, several metabolic changes must be present. These include hypocalcemia (as evidenced by the patient's prolonged QT interval), hyperphosphatemia, hyperkalemia, and hyperuricemia. Hyperphosphatemia and hyperkalemia result since both potassium and phosphate are intracellular ions, which are released after cell lysis. The subsequent increase in phosphate levels binds calcium and causes hypocalcemia. Uric acid elevation occurs due to degradation of cellular proteins. Tumor lysis syndrome can cause acute renal failure (as seen with this patient) and fatal arrhythmias.



The physician treating the 9-year-old girl in Question 5 is surprised that a medication was not administered to this patient prior to the initiation of chemotherapy to prevent tumor lysis syndrome.

Which of the following medications might have prevented this patient's renal failure?

- (A) Kayexalate
- (B) Insulin
- (C) Allopurinol
- (D) Albuterol

**The answer is C: Allopurinol.** Tumor lysis syndrome can result in acute urate nephropathy causing acute renal failure. Allopurinol has been shown to reduce the likelihood of acute urate nephropathy. Allopurinol is a purine analog that inhibits the enzyme xanthine oxidase, which prevents the production of uric acid. In addition to its use in preventing complications of tumor lysis syndrome, allopurinol is used in the treatment of chronic gout (of note, it does not treat acute gout attacks; rather it prevents attacks). Urate oxidase therapy is largely replacing allopurinol in reducing tumor lysis syndrome complications. (A, B, D) These treatments are all effective in the treatment of hyperkalemia as they all cause an intracellular potassium shift. However, even though hyperkalemia is seen in tumor lysis syndrome, these medications will have no efficacy in lowering uric acid levels and therefore not prevent acute renal failure. In other words, these medications treat the complication (hyperkalemia); they do not prevent renal failure.



A 29-year-old woman is brought to the emergency room after falling off her third floor apartment balcony. The patient suffered blunt abdominal trauma, a right femur fracture, and a left humeral fracture. On physical examination, her blood pressure is 70/30 mmHg and her heart rate is 120 beats per minute. After the administration of 5 units of packed red blood cells, the patient reports a "pins and needles"

sensation on her distal toes and around her mouth. Laboratory testing confirms a calcium level of 6.9 mg/dL and a magnesium level of 1.1 mEq/L.

Which of the following is the underlying cause of this patient's hypocalcemia and hypomagnesemia?

- (A) Exacerbation of previous hypoparathyroid state
- (B) Loss of intracellular red blood cell electrolytes during blood storage
- (C) Chelation of calcium by an anticoagulant component of packed red blood cells
- (D) Intrinsic renal failure causing hypersecretion of calcium

**The answer is C: Chelation of calcium by an anticoagulant component of packed red blood cells.**

The patient in this question is experiencing signs and symptoms of hypocalcemia and hypomagnesemia. Hypocalcemia results in paresthesia that patients often report as perioral and acral “tingling” sensations. Of note, hypocalcemia also results in hyperactive tendon reflexes and QT prolongation on ECG. Whole blood and packed red blood cells derived from whole blood contain a citrate anticoagulant that chelates serum calcium and magnesium, resulting in hypocalcemia and hypomagnesemia. (B) It is true that stored red blood cells do indeed lose intracellular potassium, but this would cause hyperkalemia. (A) The patient would likely have exhibited symptoms of hypoparathyroidism prior to her current state; furthermore, a traumatic event has never been shown to unmask hypoparathyroidism. (D) Although the patient is clearly hypovolemic, this would likely cause prerenal acute kidney injury (AKI), not intrinsic AKI.

8

A 38-year-old obese man presents with fatigue. The patient reports several bouts of daytime sleepiness in the past 6 months. He is accompanied by his wife who reports that he snores excessively each night, and that this is causing a strain on their relationship. On physical examination, the patient has a blood pressure of 158/92 mmHg and a BMI of 34 kg/m<sup>2</sup>. The rest of the physical examination is unremarkable. Laboratory studies reveal the following.

|                 |                         |
|-----------------|-------------------------|
| Leukocyte count | 8,500/mm <sup>3</sup>   |
| Hemoglobin      | 17.9 g/dL               |
| Hematocrit      | 58%                     |
| Platelets       | 290,000/mm <sup>3</sup> |

Which of the following explains this patient's laboratory abnormalities?

- (A) Hypoxemia-induced increase in erythropoietin
- (B) Myeloproliferative disorder causing myeloid cell clonal proliferation
- (C) Abnormal *BCR-ABL* fusion gene
- (D) Cobalamin deficiency

**The answer is A: Hypoxemia-induced increase in erythropoietin.** The patient in this question is presenting with signs and symptoms consistent with a diagnosis of obstructive sleep apnea (OSA). OSA is a disease with recurrent transient obstruction of the upper airway due to pharyngeal collapse. Patients tend to be overweight and complain of daytime sleepiness, snoring, headaches, and other symptoms suggesting hypertension. Importantly, OSA episodes create a state of hypoxemia that subsequently causes the kidneys to increase erythropoietin production. Erythropoietin in turn stimulates the creation of more RBCs causing polycythemia.

(B) This answer is consistent with a diagnosis of polycythemia vera, which is a primary cause of polycythemia (as opposed to hypoxemia, which is a secondary cause) that may also present with an increase in all blood cell lines. (C) This answer is consistent with a diagnosis of CML, which would cause leukocytosis (not seen with this patient). (D) Cobalamin (vitamin B<sub>12</sub>) deficiency causes megaloblastic anemia with hypersegmented neutrophils on peripheral blood smear.



A 24-year-old woman with a history of asthma presents with fatigue. She does not have a family history as she was adopted in Albania and came to the United States when she was born. The patient reports regular menstrual cycles and denies taking any medications. Laboratory studies reveal the following.

|                                           |                         |
|-------------------------------------------|-------------------------|
| Leukocyte count                           | 8,500/mm <sup>3</sup>   |
| Hemoglobin                                | 9.8 g/dL                |
| Hematocrit                                | 30%                     |
| Mean corpuscular volume                   | 70 fL                   |
| Mean corpuscular hemoglobin concentration | 27%                     |
| Platelets                                 | 290,000/mm <sup>3</sup> |

The patient is treated with iron supplementation and returns 8 weeks later without improvement in laboratory values.

Which of the following is the likely cause of this patient's condition?

- (A) Folic acid deficiency
- (B) Red blood cell enzyme deficiency
- (C) Anti-RBC antibodies
- (D) Point mutation in one of the  $\beta$ -hemoglobin genes

**The answer is D: Point mutation in one of the  $\beta$ -hemoglobin genes.** The patient in this question is presenting with microcytic anemia that is not responding to treatment with iron. Given her Mediterranean origin, she likely has  $\beta$ -thalassemia. People typically have two functional copies of the  $\beta$ -hemoglobin gene, but those with  $\beta$ -thalassemia have a point mutation in one or both of these genes (classified as minor and major, respectively). This generates reduced hemoglobin production creating a hypochromic microcytic anemia.  $\beta$ -thalassemia major results in severe and life-threatening anemia and the need for many blood transfusions, so this patient likely has the minor form. (A) Folic acid deficiency results in macrocytic megaloblastic anemia with hypersegmented neutrophils on peripheral blood smear. (B, C) These conditions cause a normocytic anemia, but this patient has a microcytic anemia (MCV <80 fL).



A 59-year-old man with a history of benign prostatic hyperplasia (BPH) presents with fatigue, decreased appetite, and a lump in his neck. The patient has smoked 1 to 2 packs of cigarettes per day for the past 30 years. On physical examination, a 2.5 cm firm and fixed nontender left submandibular mass is palpated. The rest of the examination is unremarkable. A complete blood count and comprehensive metabolic panel are within normal limits.

Which of the following is likely to be the underlying diagnosis?

- (A) Hodgkin lymphoma
- (B) Infectious mononucleosis
- (C) Squamous cell carcinoma
- (D) Papillary thyroid carcinoma

**The answer is C: Squamous cell carcinoma.** The patient in this question has an extensive history of smoking. Given the firm and nontender submandibular mass on physical examination, he likely has squamous cell carcinoma, which causes the majority of head and neck cancers. Lymph nodes that are suggestive of malignancy are hard, unilateral, and nontender. The next step in management is lymph node biopsy. (A) In chronic smokers, squamous cell carcinoma is by far the most common head and neck cancer – definitely more common than Hodgkin lymphoma. Furthermore, a patient with Hodgkin



lymphoma would likely present with generalized lymphadenopathy. (B) Infectious mononucleosis would cause a *painful* mass in the neck, not painless. Infectious mononucleosis usually causes lymphadenopathy in the posterior cervical lymph node chain. (D) This patient is not presenting with a thyroid nodule. Papillary thyroid cancer is the most common cause of thyroid cancer and has an excellent prognosis.

11

A 37-year-old man with a history of Crohn disease presents with several months of worsening fatigue. The patient reports 1 to 2 glasses of wine per night with dinner, but denies smoking or illicit drug use. Physical examination shows conjunctival pallor. Laboratory results reveal the following.

|                 |                         |
|-----------------|-------------------------|
| Leukocyte count | 5,100/mm <sup>3</sup>   |
| Hemoglobin      | 8.2 g/dL                |
| MCV             | 110 fL                  |
| Platelets       | 190,000/mm <sup>3</sup> |

The patient is started on folic acid and 4 weeks later presents with a hemoglobin level of 10.1 mg/dL. However, he reports a new “pins and needles” sensation in his distal toes and fingers.

Which of the following is the underlying cause of the patient’s CURRENT symptoms?

- (A) Inadequate treatment with folic acid
- (B) Iron deficiency
- (C) Glucose intolerance
- (D) Vitamin B<sub>12</sub> deficiency

**The answer is D: Vitamin B<sub>12</sub> deficiency.** The patient in this question likely has cobalamin (vitamin B<sub>12</sub>) deficiency. This results in megaloblastic anemia. Long-term consequences of vitamin B<sub>12</sub> deficiency include peripheral neuropathy and posterior column defects from abnormal myelin synthesis. Importantly, folic acid deficiency is another cause of macrocytic anemia and treatment with folic acid can improve the actual *anemia* of vitamin B<sub>12</sub> deficiency since both folate and vitamin B<sub>12</sub> are involved in the conversion of homocysteine to methionine. However, neurologic symptoms can be worsened in vitamin B<sub>12</sub> deficiency with the treatment of folic acid since vitamin B<sub>12</sub> is used in other biologic processes as well. As a result, it is critical to rule out vitamin B<sub>12</sub> deficiency prior to initiating folic acid. Vitamin B<sub>12</sub> deficiency results from inadequate vitamin B<sub>12</sub> intake (diet lacking in animal products) and autoimmune gastritis. The loss of gastric parietal cells secondary to autoimmune

gastritis causes intrinsic factor deficiency (which is necessary for vitamin B<sub>12</sub> absorption in the terminal ileum).

(A) The patient's underlying disorder is vitamin B<sub>12</sub> deficiency and no amount of folic acid supplementation will improve his neurologic symptoms.

(B) Iron deficiency is microcytic anemia (MCV <80 fL) and is not associated with peripheral neuropathy. (C) Although glucose intolerance commonly causes peripheral neuropathy, this patient does not have a history that suggests diabetes.

12

A 48-year-old woman with no past medical history presents with weakness and double vision for the past 7 months. The patient reports that the weakness is worse at the end of the day. Her family history is significant for hypertension and diabetes. Physical examination shows mild bilateral ptosis. Laboratory studies (thyroid studies, complete blood count, and comprehensive metabolic panel) are ordered and are all within normal limits. The patient's acetylcholine receptor antibody test is positive.

What is the best next step in the management of this patient?

- (A) Edrophonium test
- (B) CT scan of the chest
- (C) Muscle biopsy
- (D) Treatment with corticosteroids

**The answer is B: CT scan of the chest.** The patient in this question is presenting with signs and symptoms of myasthenia gravis (MG), which is confirmed with the acetylcholine receptor antibody test. This disorder manifests with weakness of the muscles (particularly at the end of the day), ptosis, and/or double vision. Shortness of breath is of serious concern in MG since respiratory muscle fatigue can lead to respiratory failure and death. After establishing the diagnosis, it is crucial to rule out a thymoma with a CT scan of the chest. Treatment of MG consists of acetylcholinesterase inhibitors and immunosuppressive drugs.

(A) The diagnosis is already established with the positive result of the acetylcholine receptor antibody test, so there is no need to perform an edrophonium test (which is less sensitive anyways). (C) Muscle biopsy can be considered if the diagnosis of MG is difficult or when myositis is suspected as the cause of the symptoms. (D) Immunosuppressive drugs are part of the treatment of MG, but the next step is to screen for thymoma in newly diagnosed MG patients.

13

A 37-year-old woman with an insignificant past medical history presents with fatigue and occasional shortness of breath for the last 9 months. The patient reports that she does not drink alcohol or smoke. Physical examination reveals a blood pressure of 100/60 mmHg, heart

rate of 104 beats per minute, and conjunctival pallor. Laboratory values reveal the following.

|                         |                         |
|-------------------------|-------------------------|
| Leukocyte count         | 5,600/mm <sup>3</sup>   |
| Hemoglobin              | 7.8 g/dL                |
| Mean corpuscular volume | 64 fL                   |
| Platelets               | 190,000/mm <sup>3</sup> |

Which of the following is the best next step in management of this patient?

- (A) Serum iron studies
- (B) Hemoglobin electrophoresis
- (C) Serum lead levels
- (D) Peripheral blood smear

**The answer is A: Serum iron studies.** The patient in this question is presenting with microcytic anemia (MCV <80 fL). The differential diagnosis of microcytic anemia can be remembered by the mnemonic “TAILS” (Thalassemia, Anemia of chronic disease, Iron deficiency anemia, Lead poisoning, Sideroblastic anemia). The most common cause of microcytic anemia is iron deficiency and the best next step is ordering iron studies: serum iron, total iron-binding capacity (TIBC), and serum ferritin. In iron deficiency anemia, serum iron is typically low, TIBC is increased, and serum ferritin is low. After iron-deficiency anemia is confirmed, the underlying cause should be determined. Iron deficiency is by far the most common cause of microcytic anemia, so a trial of iron supplementation is often performed instead of an extensive workup.

(B) Hemoglobin electrophoresis would be useful for diagnosing thalassemia.  $\beta$ -thalassemia trait usually has reduced or absent HbA, elevated levels of HbA<sub>2</sub>, and increased HbF. (C) Although lead poisoning is a cause of microcytic anemia, it is uncommon and should only be sought after iron deficiency anemia has been ruled out. (D) Peripheral blood smear is often used to exclude sideroblastic anemia, but this is an uncommon cause of microcytic anemia.

14

A 27-year-old woman presents with shortness of breath and worsening fatigue for the last month. She has a history of type 2 diabetes mellitus and mild intermittent asthma. Her family history is significant for breast cancer and hypertension. On physical examination, her blood pressure is 108/72 mmHg, heart rate is 102 beats per minute, and respiratory rate

is 14 breaths per minute. There is conjunctival pallor and scleral icterus. Laboratory results reveal the following.

|                             |                                      |
|-----------------------------|--------------------------------------|
| Leukocyte count             | 9,600/mm <sup>3</sup>                |
| Hemoglobin                  | 7.2 g/dL                             |
| MCV                         | 84 fL                                |
| Platelets                   | 192,000/mm <sup>3</sup>              |
| Total bilirubin             | 5.4 mg/dL                            |
| Direct bilirubin            | 0.9 mg/dL                            |
| Indirect bilirubin          | 4.5 mg/dL                            |
| Serum lactate dehydrogenase | 368 U/L                              |
| Serum haptoglobin           | 14 mg/dL (normal range 30–200 mg/dL) |
| Direct Coombs test          | positive                             |

Peripheral blood smear is performed and shows spherocytes without central pallor.

Which of the following is the most likely diagnosis in this patient?

- (A) Iron deficiency anemia
- (B) Hereditary spherocytosis
- (C) Autoimmune hemolytic anemia (AIHA)
- (D) Vitamin B<sub>12</sub> deficiency

**The answer is C: Autoimmune hemolytic anemia (AIHA).** The patient in this question is presenting with symptoms and signs consistent with a hemolytic anemia. Hemolytic anemias cause elevated total and indirect bilirubin, elevated LDH, and decreased haptoglobin. Pallor, icterus, and splenomegaly might be present on physical examination. The two broad categories of hemolytic anemia include intravascular hemolysis and extravascular hemolysis. In intravascular hemolysis, the RBCs are lysed within the blood vessel (i.e., mechanical valve damage or complement fixation). In extravascular hemolysis, RBCs are phagocytized by macrophages in the spleen, liver, and bone marrow. This patient's peripheral blood smear shows spherocytes without central pallor, which can be seen in both AIHA and hereditary spherocytosis. (B) However, AIHA has a positive Coombs test whereas hereditary spherocytosis has a negative Coombs test, positive osmotic fragility test, and a strong family history (it is autosomal dominant). (A) Iron-deficiency anemia causes

microcytic anemia and this patient has normocytic anemia. (D) Vitamin B<sub>12</sub> deficiency causes macrocytic anemia.

15

A 47-year-old woman who is undergoing chemotherapy for metastatic melanoma presents to the Emergency Department with fevers, chills, and weakness for the past 18 hours. The patient endorses no other complaints. She has a temperature of 39°C, blood pressure of 120/80 mmHg, heart rate of 106 beats per minute, and respiratory rate of 16 breaths per minute. Physical examination is unremarkable. Laboratory results reveal the following.

|                 |                                       |
|-----------------|---------------------------------------|
| Leukocyte count | 540/mm <sup>3</sup> (20% neutrophils) |
| Hemoglobin      | 9.2 g/dL                              |
| Platelets       | 88,000/mm <sup>3</sup>                |

A urinalysis is unremarkable and a chest x-ray shows no infiltrates.

Which of the following is the most appropriate next step in management of this patient?

- (A) Administer acetaminophen and discharge
- (B) Draw blood cultures and monitor closely
- (C) Draw blood cultures and initiate IV piperacillin–tazobactam
- (D) Draw blood cultures and initiate outpatient ciprofloxacin and amoxicillin–clavulanate

**The answer is C: Draw blood cultures and initiate IV piperacillin–tazobactam.** The patient in this question has febrile neutropenia, defined as an isolated temperature of greater than 38.3°C or sustained temperature of greater than 38.0°C for at least an hour in a neutropenic patient. Neutropenia is defined as an absolute neutrophil count (ANC) less than 1,500/mm<sup>3</sup>; it can be further characterized as mild (ANC 1,000 to 1,500/mm<sup>3</sup>), moderate (ANC 500 to 1000/mm<sup>3</sup>), or severe (ANC <500/mm<sup>3</sup>). All three classifications of febrile neutropenia require antibiotics, but only moderate and severe neutropenia require admission to the hospital for IV antibiotics. This patient has moderate febrile neutropenia and is at risk for bacterial infection from a diminished neutrophil-mediated response. Patients undergoing chemotherapy are at risk for febrile neutropenia since it alters the skin and mucosal surfaces, which can cause bacterial infection via seeding into the bloodstream. The most common site in chemotherapy-induced febrile neutropenia is the gastrointestinal tract with gram-negative organisms (especially *Pseudomonas aeruginosa*). To avoid severe sepsis, empiric antibiotic therapy must be initiated immediately.

(A, B) Blood cultures and IV antibiotics against gram-positive and gram-negative organisms is the next step in management. Antibiotics with good *Pseudomonas* coverage include piperacillin–tazobactam, meropenem, and cefepime. Of note, if MRSA is a concern (particularly in the setting of catheter-related infection, skin infection, or pneumonia), vancomycin should be added. (D) This would be the answer if the patient were mildly neutropenic, hemodynamically stable, and able to tolerate oral intake.

16

A 22-year-old woman with a history of epilepsy presents for follow-up. Other than mild fatigue, which she attributes to stress, she has no complaints. The patient has been seizure-free since initiating phenytoin therapy 3 years ago. Of note, the patient was noted to have latent tuberculosis infection after a positive PPD and has been taking isoniazid for the past 5 months. Physical examination is unremarkable. Laboratory results reveal the following.

|                         |                         |
|-------------------------|-------------------------|
| Leukocyte count         | 9,100/mm <sup>3</sup>   |
| Hemoglobin              | 10.5 g/dL               |
| Mean corpuscular volume | 104 fL                  |
| Platelets               | 210,000/mm <sup>3</sup> |

Which of the following underlying mechanisms likely explains the laboratory findings?

- (A) Impaired absorption of folic acid
- (B) Intrinsic factor depletion due to autoimmune destruction of parietal cells
- (C) Excessive bleeding during menstrual cycle
- (D) Isoniazid depletion of vitamin B<sub>6</sub>

**The answer is A: Impaired absorption of folic acid.** The patient in this question is presenting with macrocytic anemia. Various causes of megaloblastic anemia include folic acid deficiency, vitamin B<sub>12</sub> deficiency, and drug-induced (HIV medications, trimethoprim, sulfamethoxazole, oral contraceptives, and anticonvulsants). The patient is taking phenytoin, which along with primidone and phenobarbital, can cause a megaloblastic anemia by impairing the absorption of folic acid in the small intestine. Accordingly, this patient should initiate folate supplementation. (B) Intrinsic factor depletion due to autoimmune destruction of parietal cells would cause a vitamin B<sub>12</sub> deficiency that also causes a macrocytic anemia. However, there is nothing in this patient's history that supports vitamin B<sub>12</sub> deficiency. (C) Excessive menstrual bleeding

would cause iron-deficiency anemia. (D) Although isoniazid is associated with decreased vitamin B<sub>6</sub> levels, this is not a cause of macrocytic anemia. Instead, it can cause peripheral neuropathy.

17

A 41-year-old woman with an insignificant past medical history presents for her annual check-up. The patient is very anxious because she has had a vague abdominal pain for the past 3 months. She reports that this mild abdominal pain started after she read online about ovarian cancer. She was researching the disease since her best friend's mother was diagnosed with stage IV ovarian cancer. The patient is very concerned because she was informed that her paternal aunt passed away from ovarian cancer. The patient denies fevers, chills, weight loss, fatigue, or any other systemic symptom. Her Pap smear 2 years ago was normal.

Which of the following screening options should be recommended for this patient?

- (A) Annual serum CA 125 levels
- (B) Annual transvaginal ultrasound
- (C) Annual pelvic examination
- (D) No specific screening measures recommended

**The answer is D: No specific screening measures recommended.**

Ovarian cancer has the highest mortality rate in the United States of all the gynecologic malignancies. Pelvic ultrasound and serum CA 125 levels are helpful in making a diagnosis of ovarian cancer in patients who have symptoms and/or findings on physical examination. Nonetheless, there is no evidence in the medical literature that screening for ovarian cancer with ultrasound or CA 125 levels actually reduces mortality. In patients with a *very* strong family history of ovarian cancer, testing for the BRCA1 and BRCA2 genes is certainly an option. For women who test positive for one of the BRCA genes, pelvic ultrasound and serum CA 125 levels are an appropriate next step. Importantly, CA 125 is best used for tracking disease progression and recurrence *after* the diagnosis has been made. However, this patient only presents with a family history of one paternal aunt who passed from ovarian cancer. In patients with average risk, such as this patient, no screening is currently recommended.

18

A 31-year-old man presents with progressive dyspnea with exertion, dry cough, and fatigue. He started chemotherapy 2 months previously for advanced testicular cancer. The patient reports that his symptoms have worsened since starting chemotherapy. Physical examination reveals fine inspiratory crackles at the lung bases on auscultation. A high-resolution CT is ordered which shows extensive fibrosis.

Which chemotherapeutic agent is the likely cause of this patient's symptoms?

- (A) Cyclophosphamide
- (B) Bleomycin
- (C) Cisplatin
- (D) Vincristine

**The answer is B: Bleomycin.** This patient has developed pulmonary fibrosis as a result of chemotherapy, likely from bleomycin. The drug is used in the treatment of Hodgkin lymphoma (as a component of the ABVD and BEACOPP regimen), squamous cell carcinomas, and testicular cancer. The mechanism of action involves breaking DNA. The most severe side effect of bleomycin is pulmonary fibrosis and abnormal lung function. (A) Cyclophosphamide is typically used in the treatment of lymphomas, brain cancer, and leukemia. The mechanism involved is inducing the death of T cells. Although cyclophosphamide has several severe side effects, the most testable and unique one is hemorrhagic cystitis. (C) Cisplatin is a platinum-containing chemotherapeutic agent that binds to and causes crosslinking of DNA, which triggers apoptosis. The most testable side effects of cisplatin (and carboplatin) are nephrotoxicity and ototoxicity. (D) Vincristine inhibits assembly of microtubules and arrests cells in metaphase of mitosis. The most common and testable side effect of vincristine is peripheral neuropathy.



- 19 A 62-year-old woman presents with abdominal pain and bloating for the past 18 hours. The patient also endorses nausea and diarrhea. On physical examination, she has a temperature of 38.5°C, blood pressure of 80/52 mmHg, heart rate of 75 beats per minute, and respiratory rate of 16 breaths per minute. Abdominal distention and diffuse abdominal tenderness to palpation are present and fecal occult blood test is positive. The patient is started on IV normal saline and IV antibiotics. Further laboratory values reveal the following.

|                         |                         |
|-------------------------|-------------------------|
| Leukocyte count         | 42,100/mm <sup>3</sup>  |
| Hemoglobin              | 13.5 g/dL               |
| Mean corpuscular volume | 88 fL                   |
| Platelets               | 320,000/mm <sup>3</sup> |
| Sodium                  | 138 mEq/L               |
| Potassium               | 3.7 mEq/L               |
| Bicarbonate             | 17 mEq/L                |
| Creatinine              | 1.2 mg/dL               |



Leukocyte alkaline phosphatase score is elevated.

Which of the following is the most likely diagnosis in this patient?

- (A) Chronic lymphocytic leukemia
- (B) Chronic myelogenous leukemia
- (C) Leukemoid reaction
- (D) Myelodysplastic syndrome

**The answer is C: Leukemoid reaction.** The patient in this question is presenting with hemodynamic instability and severe leukocytosis. Severe leukocytosis can indeed suggest an underlying leukemia, but this patient presents with an elevated leukocyte alkaline phosphatase (LAP) score. A leukemoid reaction causes severe leukocytosis due to infection or inflammation. LAP scores are elevated in leukemoid reaction. (B) To distinguish leukemoid reaction from CML, it is critical to order a LAP score. LAP scores are *depressed* in CML. Nonetheless, it is important to note that sometimes LAP scores are elevated in CML when there is secondary infection. In this case it is critical to perform cytogenetic studies to look for abnormal chromosome 22 and presence of the Philadelphia chromosome. This patient does not present with systemic symptoms that suggest CML. (A) Chronic lymphocytic leukemia (CLL) will also present with decreased LAP scores. Furthermore, lymphocytes are predominant in CLL. (D) Myelodysplastic syndrome presents with pancytopenia, which does not reflect this patient's laboratory values.

20

A 22-year-old man presents with bloody and tarry stools for the last month. The patient denies any associated symptoms and reports that he does not know his family history since he is adopted. Fecal occult blood test is positive and the patient has a hemoglobin level of 8.9 g/dL. Colonoscopy is performed and hundreds of colonic polyps are appreciated. Biopsy confirms that they are adenomatous polyps.

What is the best next step in management for this patient's condition?

- (A) Reassurance as the polyps are benign
- (B) Repeat colonoscopy and biopsy in 1 year
- (C) Monthly FOBT and CEA levels
- (D) Elective proctocolectomy

**The answer is D: Elective proctocolectomy.** This patient is presenting with symptoms, signs, and colonoscopic findings consistent with a probable diagnosis of familial adenomatous polyposis (FAP). Although we do not have this patient's family history, FAP is autosomal dominant and is caused by genetic mutations in the adenomatous polyposis coli (APC) gene. This mutation results in abnormal tumor suppressor genes that normally prevent the

development of tumors. FAP causes numerous adenomatous polyps to form mainly in the epithelium of the large intestine. Of note, this is not a common condition and accounts for less than 1% of colon cancer cases. This patient, who presents with hundred of adenomatous polyps, has a 100% risk of cancer. Therefore, the appropriate course of action is to perform proctocolectomy. (A, B, C) Surveillance is not encouraged with FAP as there is a 100% risk of colon cancer. Proctocolectomy must be performed at the time of diagnosis to prevent malignant transformation.

## Neurology

1

A 37-year-old woman with a history of multiple sclerosis presents for follow-up. Since her previous visit 7 months ago, she has had a few episodes of monocular vision impairment and weakness and incoordination in her right upper extremity. Although these symptoms resolved completely, she reports that one episode of vision impairment 2 months ago was so severe that she was admitted to the hospital and received intravenous corticosteroids.

Which of the following is often used to decrease the frequency of relapse and slow the progression of this patient's disorder?

- (A) Methotrexate
- (B) Interferon- $\beta$
- (C) High-dose corticosteroids
- (D) Cyclosporine

**The answer is B: Interferon- $\beta$ .** The patient in this question has multiple sclerosis (MS), specifically the relapsing–remitting form. Relapsing–remitting MS involves unpredictable attacks followed by periods of remission. Interferon- $\beta$  has been shown to be effective in several clinical trials for the relapsing–remitting form of MS in that it decreases the frequency of relapse and reduces overall disability in patients. (A, D) Methotrexate and cyclosporine are immunosuppressive medications that are often used in the *primary progressive* form of MS. This type of MS is characterized by a steady decrease in disability without obvious remissions. In the progressive form of MS, these medications are helpful in stopping such a rapid course of the disease, but provide only temporary relief and have not been shown to offer long-term benefits. Other types of MS include *secondary progressive* in which an initial relapsing–remitting MS suddenly declines without periods of remission and *progressive relapsing* in which there is a steady decline after the onset of symptoms with superimposed attacks. (C) High-dose corticosteroids are the first line for acute attacks of all types of MS. They do not slow down the long-term progression of the disease.

2

A 33-year-old woman presents with a severe headache that began 5 hours ago. The patient reports that the headache is unilateral on the left side and endorses nausea, an episode of vomiting, and photophobia. Neurologic examination reveals normal muscle strength and no sensory loss.

Which of the following is the best next step in the management of this patient?

- (A) Propranolol
- (B) Amitriptyline
- (C) Chlorpromazine
- (D) Verapamil

**The answer is C: Chlorpromazine.** The patient in this question is likely having an acute episode of a *migraine headache*. Migraines are characterized by unilateral, pulsating pain that is often associated with photophobia and an aura of neurologic symptoms prior to the onset of the headache. Acute attacks can range in duration from 4 to 72 hours. Acute treatment and primary preventive treatment vary in migraine headaches. Acute attacks are best treated with intravenous antiemetic medications (chlorpromazine and prochlorperazine) and/or triptans (sumatriptan). The American Academy of Neurology actually recommends NSAIDs and caffeine/acetaminophen as first-line treatment for mild-moderate migraines. However, chlorpromazine is the right answer for this question since this patient's symptoms are consistent with a moderate-severe migraine (vomiting, photophobia). Given that this patient presents with vomiting, chlorpromazine is the best choice since it can be given in IV form.

(A, B) Propranolol and amitriptyline are both excellent medications used for migraine *prophylaxis*, not for acute episodes. These would be appropriate to give to the patient after her acute migraine episode resolves to prevent further attacks. (D) Verapamil is a calcium channel blocker that is the first-line medication for *cluster headache* prophylaxis. However, this patient is having a migraine, not a cluster headache. Cluster headaches typically involve pain around the eye with eye watering, nasal congestion, and swelling. Cluster headaches are much more common in men and acute treatment involves inhaled oxygen and sumatriptan.

Finally, another commonly tested type of headache is a *tension headache*, which is bilateral and typically involves greater than 30 minutes of pain without photophobia or aura. Tension headaches respond well to NSAIDs; however, amitriptyline can be given for chronic tension headaches.

3

A 53-year-old man presents to the hospital accompanied by police officers. He was found walking in the middle of a very busy highway. When asked for his name, age, time, and place, his responses are unintelligible. He has a blood pressure of 154/92 mmHg and a heart rate of 94 beats

per minute. Physical examination shows a malnourished patient with dilated pupils that are reactive to light. The patient is noted to have an ataxic broad-based gait.

Which of the following is the best initial treatment for this patient?

- (A) Haloperidol
- (B) Naloxone
- (C) Thiamine
- (D) Clonidine

**The answer is C: Thiamine.** This patient is presenting in a disoriented and confused state; the differential is broad and includes infection, intoxication, vitamin deficiency, hypoxia, and several other neurologic conditions. In clinical scenarios in which the patient's history is limited, the provider must immediately attempt to treat reversible causes of confusion. The treatment of choice includes thiamine (for Wernicke encephalopathy), dextrose (for hypoglycemia), oxygen (for hypoxia), and naloxone (for opiate overdose).

Although the aforementioned regimen is appropriate to cover all potential sources, this question only offers one possible treatment and therefore clinical clues are critical here. Given this patient's ataxia, Wernicke encephalopathy should be suspected. Wernicke encephalopathy typically presents with confusion, ataxia, and ophthalmoplegia and results from a deficiency of thiamine (vitamin B<sub>1</sub>). It commonly occurs in alcoholic patients with poor nutrition. Of note, patients should receive thiamine *before* dextrose, since this can actually worsen or even precipitate Wernicke encephalopathy. (A) Haloperidol is a typical antipsychotic medication used in the treatment of schizophrenia and psychotic states. This is not used in the treatment of reversible causes of confusion. (B) Although naloxone (opiate antagonist) is used in the treatment of reversible causes of confusion to cover opiate intoxication, it would present with pinpoint pupils and respiratory depression, which are not seen in this patient. (D) Clonidine is an antihypertensive medication (acts on central  $\alpha$ -receptors). Although this patient is hypertensive, blood pressures typically need to be higher than 180/120 mmHg to cause hypertensive encephalopathy.



A 43-year-old HIV positive man presents with new onset right-sided paralysis. He recently started trimethoprim-sulfamethoxazole (TMP-SMX) for a CD4 count of 70/mm<sup>3</sup>. The patient is afebrile and vital signs are within normal limits. Neurologic examination demonstrates hyper-reflexia, hypertonia, and positive Babinski sign on the right side.

Which of the following is the most likely diagnosis in this patient?

- (A) Progressive multifocal leukoencephalopathy (PML)
- (B) Primary CNS lymphoma
- (C) AIDS dementia complex
- (D) Toxoplasmosis

**The answer is A: Progressive multifocal leukoencephalopathy (PML).**

The patient in this question is likely suffering from PML, an opportunistic infection seen in immunocompromised patients that is caused by the JC virus (a human polyomavirus that has an unknown mode of transmission). This disease typically involves cortical white matter and does not produce a mass effect. Symptoms typically include hemiparesis, speech disturbances, and vision and gait changes. CT scan shows several nonenhancing cerebral demyelinating white matter lesions without any mass effect. There is no treatment for PML and the prognosis is poor. **(B)** Primary CNS lymphoma is the second most common cause of mass lesions (following toxoplasmosis) in HIV-infected patients. This involves a *ring-enhancing* lesion that is solitary and typically periventricular. The diagnosis is confirmed by EBV DNA in the cerebrospinal fluid (CSF). **(C)** AIDS dementia complex will demonstrate cortical atrophy and ventricular enlargement. **(D)** Toxoplasmosis is the most common *ring-enhancing* mass lesion in HIV-infected patients. Lesions are multiple, spherical, and typically located in the basal ganglia. This is unlikely given that the patient is currently taking TMP-SMX.

5

A 63-year-old woman with a history of hypertension presents with worsening memory over the past 5 months. Her husband reports that recently she had forgotten to turn off the oven a few times and has forgotten several appointments, which is unusual for her. The patient also endorses urinary incontinence and “clumsiness.” The patient’s hypertension is well-controlled on hydrochlorothiazide. Physical examination shows that her blood pressure is 128/84 mmHg and her pulse is 76/min. Neurologic examination is within normal limits except for a broad-based gait.

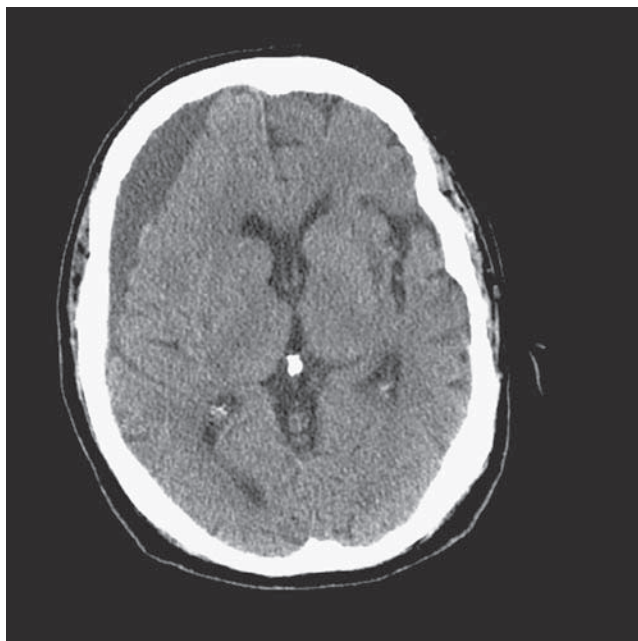
Which of the following is the most likely diagnosis?

- (A)** Pseudotumor cerebri
- (B)** Alzheimer disease
- (C)** Normal pressure hydrocephalus
- (D)** Multi-infarct dementia

**The answer is C: Normal pressure hydrocephalus.** The patient in this question is presenting with dementia, urinary incontinence, and gait disturbance. This triad, often remembered by “wet, wacky, wobbly,” is characteristic of normal pressure hydrocephalus (NPH). NPH is diagnosed by MRI, which will show dilated ventricles. As one would expect from the name, the opening pressure measured during lumbar puncture is normal. Treatment generally consists of repeated spinal taps to improve the symptoms (by decreasing the pressure exerted on the adjacent cortical tissue by the enlarged ventricles). **(B)** Alzheimer disease is not associated with gait problems or urinary incontinence. **(A)** Pseudotumor cerebri is associated with headaches, not memory impairment or dementia. Furthermore, it is typically seen in young, obese females. **(D)** Although this patient has a history of hypertension, it is well-controlled and

thus her symptoms are unlikely to be a result of multi-infarct dementia. This type of dementia tends to be very abrupt in onset and show multiple areas of increased T2-weighted density on MRI in the periventricular regions.

- 6** A 67-year-old woman with an insignificant past medical history presents with her husband who reports that she has become increasingly confused over the past week. The husband reports that she had a “hard fall” down a few stairs 10 days ago and since then has been hesitant to walk. A contrast-enhanced head CT is ordered and is shown in *Figure 8-1*.



**Figure 8-1**

Which of the following is the underlying cause of this patient's condition?

- (A) Tearing of the middle meningeal artery
- (B) Tearing of the bridging veins
- (C) Ruptured aneurysm
- (D) Hypertensive hemorrhage

**The answer is B: Tearing of the bridging veins.** This patient is suffering from a subdural hematoma, which is caused by blunt trauma that tears the bridging veins, which connect the cortical superficial veins to the sagittal sinus

in the dura. This blood will *slowly* extravasate into the subdural space, which is why this patient's fall was recorded over a week prior to admission. Epidural hematomas, on the other hand, become immediately symptomatic (although the classic description of epidural hematomas is that of a "lucent" phase followed by rapid decline). Subdural hematomas manifest symptomatically with headache and gradual confusion and loss of consciousness. Of note, subdural hematomas are much more common in elderly patients and alcoholic patients (brain atrophy and fragility of vasculature). Radiologic findings of a subdural hematoma include a white crescent on noncontrast CT of the head. Also, a midline shift is commonly appreciated. Treatment is neurosurgic hematoma evacuation. (A) Tearing of the middle meningeal artery is the underlying cause of most epidural hematomas. (C) Ruptured aneurysm is the underlying cause of a subarachnoid hemorrhage. (D) In addition to the radiologic evidence, this particular patient has an insignificant past medical history and therefore hypertensive hemorrhage is not the right answer.



A 57-year-old man presents with new onset left-sided weakness, urinary incontinence, and left leg "heaviness" for the past 5 hours. That patient has a long history of diabetes and is noncompliant with his medications. Neurologic examination reveals 3/5 strength in the left upper extremity and 1/5 strength in the left lower extremity. Sensation to pinprick and fine touch is markedly diminished over the left leg. Visual field testing is within normal limits.

Which of the following is the most likely location of this patient's stroke?

- (A) Right middle cerebral artery
- (B) Left middle cerebral artery
- (C) Right anterior cerebral artery
- (D) Left anterior cerebral artery

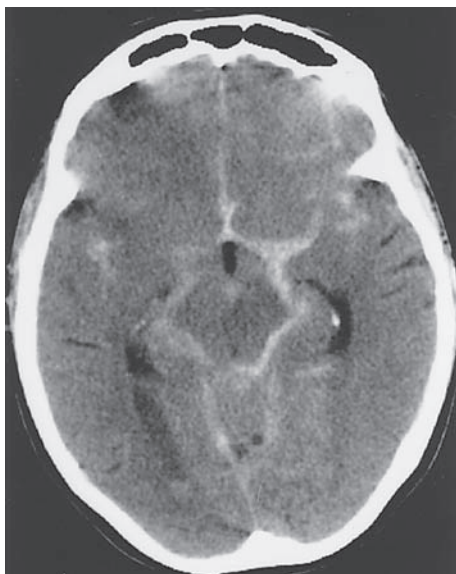
**The answer is C: Right anterior cerebral artery.** This patient is suffering from a stroke and this question asks to localize the location of the stroke. Strokes are either hemorrhagic (secondary to subarachnoid hemorrhage or intracerebral hemorrhage) or ischemic (secondary to embolism, thrombosis, or hypoperfusion). This patient is having a stroke of the right anterior cerebral artery. This is characterized by *contralateral* motor and/or sensory deficits that are particularly symptomatic in the lower limb (as seen in this patient). Another clue to anterior cerebral artery strokes includes urinary incontinence.

(A, B) Middle cerebral artery strokes manifest as *contralateral* motor and/or sensory deficits that are particularly symptomatic in the upper limb (rather than the lower limb as seen in this patient). Furthermore, if the dominant lobe (usually left) is involved in the stroke, the patient may present with aphasia. (D) Left anterior cerebral artery strokes would demonstrate symptomatically on the right side.



8

A 37-year-old woman presents with a severely intense headache that began a few hours ago. The headache has not improved since then and the patient has vomited several times. She reports that it is diffusely painful, and she is unable to recall if any “funny sensations” occurred prior to the headache. She does not report head trauma or fever. The patient is too uncomfortable to tolerate a thorough neurologic examination and a CT scan of the head is ordered (*Figure 8-2*).



**Figure 8-2**

Which of the following is the underlying cause of this patient's headache?

- (A) Venous sinus thrombosis
- (B) Ruptured berry aneurysm
- (C) Arteriovenous malformation
- (D) Amyloid angiopathy

**The answer is B: Ruptured berry aneurysm.** This patient is likely suffering from a nontraumatic subarachnoid hemorrhage as evidenced by the noncontrast head CT scan. CT scan findings in a subarachnoid hemorrhage include bright (hyperdense) signals that represent *acute* bleeding (usually in the cisterns). In the case of nontraumatic subarachnoid hemorrhages, the most common cause is ruptured berry or saccular aneurysms. Rupture is more likely for aneurysms greater than 7 mm. Of note, if this patient presented with a negative

head CT and a subarachnoid hemorrhage was still suspected, the next best step is to perform a lumbar puncture, which will demonstrate xanthochromia.

(A) Venous sinus thrombosis typically presents with *progressively* worsening headache and causes hemorrhage along the major cerebral draining veins. (C) Arteriovenous malformation is also a cause of subarachnoid hemorrhages (and intracerebral hemorrhages), but the most common cause of nontraumatic subarachnoid hemorrhages is a ruptured aneurysm. (D) Amyloid angiopathy is the second most common cause of intracerebral hemorrhage. However, this type of hemorrhage is *lobar* in its location and results from abnormal  $\beta$ -pleated amyloid protein deposition in the cerebral blood vessels.

9

A 27-year-old woman presents with fatigue and double vision. The patient reports that these symptoms occur at the end of a “long work day.” The patient also reports that she does not eat “tough” foods anymore such as steak or chicken as it is difficult for her to chew. Neurologic examination is unremarkable and the patient has normal thyroid-stimulating hormone (TSH) and creatine kinase (CK) levels. The diagnosis is confirmed with a special laboratory test.

Which of the following is the next best step in management of this patient?

- (A) MRI of the head
- (B) CT scan of the chest
- (C) CT scan of the abdomen
- (D) Ultrasound of the neck

**The answer is B: CT scan of the chest.** The patient in this question is suffering from myasthenia gravis (MG), an autoimmune neuromuscular disease leading to fluctuating muscle weakness and fatigue. The main symptom of MG is muscle weakness *after* a period of muscle use. Extraocular muscles are commonly involved leading to double vision. Jaw fatigue is common as well due to fatigue of the bulbar muscles. The underlying mechanism of MG is circulating antibodies that block acetylcholine receptors at the postsynaptic neuromuscular junction. In contrast, Lambert-Eaton syndrome has autoantibodies directed at presynaptic voltage-gated calcium channels. Of note, about 15% of patients with MG will have a thymoma, so it is critical to perform a CT scan of the chest after the diagnosis is made. (A, C, D) These are not the most appropriate first steps in management after the diagnosis of MG is made. A thymoma must first be excluded since it can become invasive.

10

A 26-year-old man presents with symmetric ascending weakness of the bilateral lower extremities. The patient also endorses numbness and tingling in his toes and reports that he had a diarrheal episode

7 days ago that lasted for 2 days. Neurologic examination confirms symmetric weakness in the lower extremities with diminished and delayed reflexes. Electrophysiologic studies confirm slowing of nerve conduction velocities.

Which of the following pathogens is likely to be the cause of this patient's disorder?

- (A) *Shigella*
- (B) *Escherichia coli* (O157: H7)
- (C) *Salmonella*
- (D) *Campylobacter jejuni*

**The answer is D: *Campylobacter jejuni*.** This patient is suffering from Guillain-Barré syndrome (GBS), an acute polyneuropathy associated with ascending paralysis. The majority of patients will report a respiratory or gastrointestinal infection that preceded the neurologic symptoms. GBS is an autoimmune disease resulting from an immune response to foreign antigens that incorrectly targets host nerve tissues through a mechanism known as molecular mimicry. The most common infectious agent and precipitant of GBS is *Campylobacter*, so this is likely to be the pathogen causing this patient's diarrheal episode. (A, B, C) These are pathogens that also cause gastrointestinal infections, but these are not likely to cause GBS. Other precipitants of GBS include herpes simplex virus (HSV), *Mycoplasma*, and *H. influenzae*.



A 46-year-old man presents with numbness in his distal fingertips. The patient rarely seeks medical attention and has an insignificant past medical and family history. The patient reports drinking 6 to 7 beers per week and smoking a half pack of cigarettes per day. During neurologic examination, the patient is asked to extend his arms with his eyes shut and maintain his palms facing up. During this maneuver, the patient's arms both pronate.

Based on the above finding, which of the following is impaired in this patient?

- (A) Proprioception
- (B) Upper motor neuron pathway
- (C) Tactile sensation
- (D) Cerebellar function

**The answer is B: Upper motor neuron pathway.** This patient is exhibiting pronator drift on neurologic examination. This is both a *specific* and *sensitive* test for upper motor neuron (UMN) disease. UMN disease will very often cause a weakness in supination that allows the pronating muscles to become more dominant. Therefore, when patients are asked to close their eyes and

stretch out their arms with their palms facing upward, the affected arm(s) will pronate.

(A) Proprioception can be assessed in various physical examination maneuvers. One of the more common ways to evaluate proprioception is with the Romberg test in which the patient stands with his or her feet together and the practitioner observes if the patient is able to maintain balance with their eyes closed. Patients with impaired proprioception will lose their balance. (C) Although this patient presents with “numbness,” which might lead the reader to the false conclusion that he has peripheral neuropathy leading to impaired tactile sensation (measured by pinprick discrimination), this maneuver was not explicated in the question. (D) Cerebellar function is responsible for balance and coordination and can be assessed by testing for rapidly alternating movements.

12

A 26-year-old man presents with a stabbing, severe pain in the left side of his face for the past 2 weeks. The pain is described as a “stabbing knife” sensation and occurs about every 12 to 15 minutes. It lasts for about 4 to 5 seconds. The pain is so unbearable that the patient cannot sleep or function in his employment as an accountant. The patient has tried aspirin and acetaminophen to no avail. Physical examination is unremarkable, but the patient has one of the attacks during the visit and visibly shows excruciating pain.

Which of the following is the treatment of choice for this patient’s condition?

- (A) Sumatriptan
- (B) Acyclovir
- (C) Morphine
- (D) Carbamazepine

**The answer is D: Carbamazepine.** This patient is presenting with signs and symptoms consistent with a diagnosis of trigeminal neuralgia, a neuro-pathic disorder characterized by episodes of intensely severe pain in the face that originates from the trigeminal nerve. The drug of choice for trigeminal neuralgia is carbamazepine, an anticonvulsant that stabilizes the inactivated state of voltage-gated sodium channels. The drug is effective in the majority of patients with trigeminal neuralgia; however, one of the rare side effects is aplastic anemia so routine complete blood count (CBC) is necessary with these patients. If carbamazepine fails to alleviate the pain, surgery through decompression or partial resection of the trigeminal nerve is the next best option. (A) Sumatriptan is used in acute migraine attacks and cluster headaches. (B) Acyclovir is used in the treatment of herpes zoster and herpetic neuralgia. However, this presents with pain and a vesicular rash in a dermatomal distribution. (C) Morphine is a narcotic agent used to control pain in

several disorders. It has not been shown to be of benefit in patients suffering from trigeminal neuralgia.

- 13** A 36-year-old woman presents with a 2-day history of fever, stiff neck, and headaches. She also was reported to have had one seizure just prior to her admission. The patient has a temperature of 39°C, blood pressure of 120/80 mmHg, and heart rate of 106 beats per minute. A lumbar puncture is performed and her CSF studies reveal the following.

|                  |                         |
|------------------|-------------------------|
| Opening pressure | 218 mm H <sub>2</sub> O |
| Protein          | 210 mg/dL               |
| Glucose          | 58 mg/dL                |
| Leukocytes       | 160/mm <sup>3</sup>     |
| Lymphocytes      | 92%                     |
| Neutrophils      | 8%                      |
| RBC              | 220/mm <sup>3</sup>     |

Which of the following is the most likely diagnosis in this patient?

- (A) Meningococcal meningitis
- (B) Herpes simplex encephalitis
- (C) Tuberculous meningitis
- (D) Pneumococcal meningitis

**The answer is B: Herpes simplex encephalitis.** This question is testing one's ability to distinguish causes of abnormal CSF values. The patient in this question likely has herpes simplex (HSV) encephalitis, which accounts for almost 20% of viral encephalitis cases and presents with fever, focal seizures, and sometimes aphasia, ataxia, hemiparesis, and behavioral symptoms. HSV encephalitis typically affects the temporal lobes of the brain and has an acute onset. CSF analysis is critical in securing the diagnosis. CSF studies reveal lymphocytosis, elevated protein levels, normal glucose levels, and occasionally increased levels of RBCs due to hemorrhagic destruction of the temporal lobes. To solidify the diagnosis, the most specific test is PCR analysis of HSV DNA in the spinal fluid.

(A, D) Bacterial meningitis will present with *low* glucose in the CSF. In addition, rather than lymphocytosis, increased neutrophils will be seen on CSF analysis. (C) Fungal meningitis often presents with *low* glucose like bacterial

meningitis, but will accompany a lymphocytosis. The patient in this question has a CSF analysis that is consistent with a viral etiology.

- 14** A 56-year-old man presents for evaluation of a tremor. The patient reports that over the last 6 months he has been having tremors in both hands that appear to improve with alcohol intake. The patient denies any tremors at rest. The tremor is worsened when he reaches for his coffee cup in the cupboard each morning. The patient reports that his father appeared to be “shaky” but does not recall his exact diagnosis since he passed when the patient was very young. Physical examination demonstrates a tremor that increases in amplitude at the end of goal-directed activities (reaching for a piece of paper).

Which of the following is the medication of choice for this patient's condition?

- (A) Propranolol
- (B) Trihexyphenidyl
- (C) Haloperidol
- (D) Primidone

**The answer is A: Propranolol.** The patient in this question is presenting with signs and symptoms consistent with a diagnosis of essential tremor, which is inherited in an autosomal dominant fashion. The distal upper extremities are typically affected and the legs are usually not involved. The tremor increases in amplitude when the arms are outstretched. The drug of choice for essential tremor is propranolol, with clonazepam being a second-line treatment. (B) Trihexyphenidyl is an anticholinergic used in the treatment of the resting tremor seen in Parkinson disease. (C) Haloperidol is the treatment used in Huntington disease, but this disease is characterized by several symptoms including chorea and dementia that are not seen in this patient. (D) Although primidone can be used in the treatment of essential tremor, it is typically used in combination with propranolol.

- 15** A 44-year-old woman presents with a 5-month history of headaches and weight loss. The headache is diffusely painful and is markedly worse when the patient coughs or bends over. The patient has vomited several times over the last few months. Neurologic examination reveals papilledema on fundoscopy. An MRI of the head is ordered and shows the following (*Figure 8-3*).

Which of the following is the most likely diagnosis?

- (A) Low-grade astrocytoma
- (B) Meningioma
- (C) Glioblastoma multiforme
- (D) Metastatic brain tumor

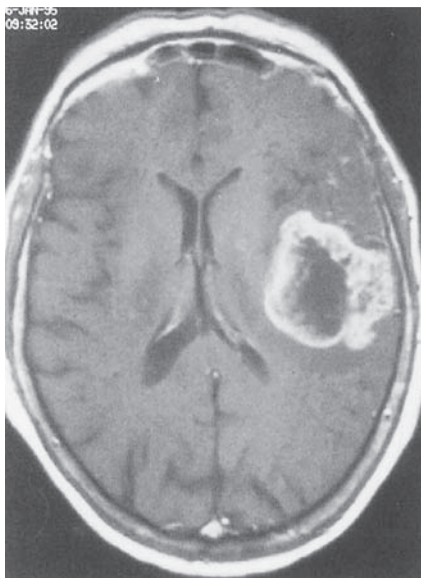


Figure 8-3

**The answer is C: Glioblastoma multiforme.** The patient in this question is presenting with a classic description of the most common primary brain tumor, glioblastoma multiforme (GBM). Headaches that worsen with changes in position and that are associated with nausea, vomiting, and weight loss raise the flag of increased intracranial pressure from a space-occupying lesion. A “butterfly”-appearing ring-enhancing lesion (straddling and extending across the corpus callosum) with central necrosis is the classic MRI finding in GBM. Unfortunately, GBM is not only the most common primary brain tumor, but also the most aggressive with survival time typically less than 6 months.

(A) Low-grade astrocytomas are more common in children and usually present with seizures. (B) Meningiomas are benign tumors that arise from the meninges. Many are asymptomatic and do not require treatment. Symptomatic meningiomas can be surgically removed. (D) Although metastatic brain tumors are the most common tumor (not a *primary* tumor such as GBM) found in the brain, the site of metastases is the gray–white junction of the cerebrum. Furthermore, metastases are typically multifocal and spherical.





## Rheumatology

1

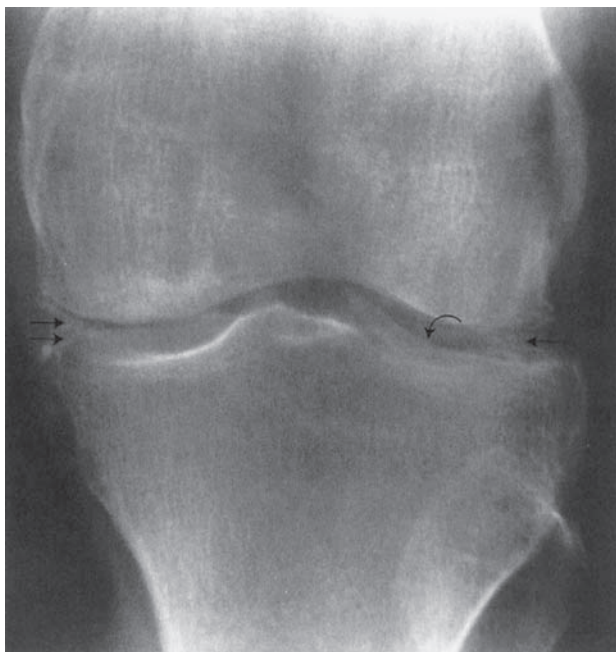
A 71-year-old man with a history of hypertension and hyperlipidemia presents with severe left knee pain and fever. Physical examination demonstrates a swollen left knee with limited range of motion. The patient is noted to have a temperature of 38.8°C and a blood pressure of 150/100 mmHg. Synovial fluid is drawn from the left knee and reveals the following.

|                 |                                          |
|-----------------|------------------------------------------|
| Leukocyte count | 28,000/mm <sup>3</sup> (94% neutrophils) |
| Crystals        | Positively birefringent, rhomboid-shaped |
| Gram stain      | Negative                                 |

Which of the following is likely to be present in this patient's condition?

- (A) Calcification of articular cartilage
- (B) Rheumatoid factor
- (C) Tophi
- (D) *S. aureus* bacteremia

**The answer is A: Calcification of articular cartilage.** The patient in this question is showing signs and symptoms of pseudogout, an acute arthritis that is caused by calcium pyrophosphate dihydrate (CPPD) crystal release from calcified articular cartilage into the joint space. This calcification of articular cartilage is referred to as chondrocalcinosis and often manifests with pain, swelling, erythema, fever, and limited range of motion. The knee is the most common joint that is affected in pseudogout (*Figure 9-1* demonstrates articular cartilage calcification on x-ray).



**Figure 9-1**

Of note, even though fever and leukocytosis (often with left shift as seen in this patient) can occur in pseudogout, they are not required for the diagnosis. Diagnosis of pseudogout relies on identifying rhomboid-shaped positively birefringent crystals on synovial fluid analysis. An approach to the initial differential diagnosis of arthritis is shown below in *Figure 9-2*.

**(B)** Rheumatoid factor (RF) typically occurs in rheumatoid arthritis (RA); however, a positive RF does not make the diagnosis of RA as RF can be positive in several other conditions. RA is characterized by a symmetric arthritis of insidious onset. Fever can be present as well. **(C)** Tophi are characteristic of gout (specifically chronic gout) and are urate crystals that manifest as yellowish nodules of firm consistency at affected joints (*Figure 9-3*). Gout is diagnosed by needle-shaped, *negatively* birefringent crystals on synovial fluid analysis. **(D)** *S. aureus* bacteremia with arthritis would characterize septic arthritis (*S. aureus* is the most common cause). Even though this patient presents with fever and leukocytosis, the identification of rhomboid-shaped positively birefringent crystals leads to the diagnosis of pseudogout. Furthermore, the gram stain is negative with this patient.

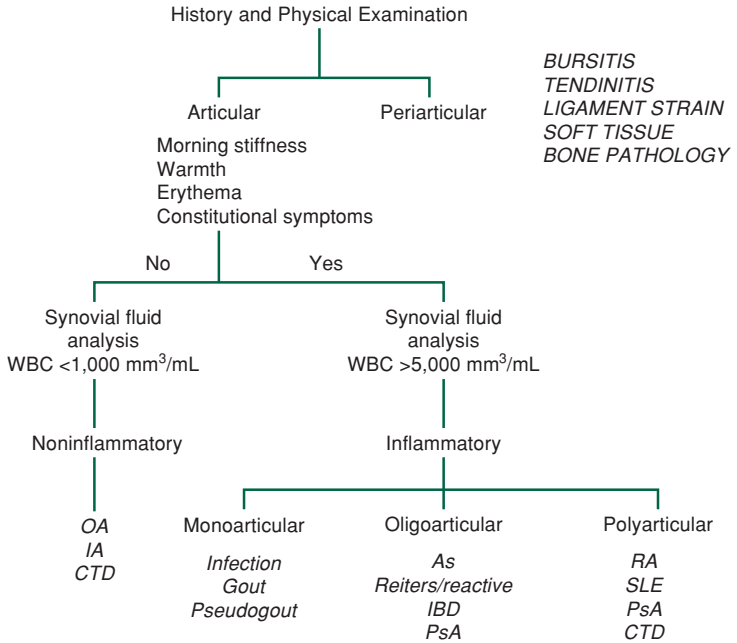


Figure 9-2



Figure 9-3

2

A 68-year-old man presents with pain in his shoulders, hips, and neck for the last 5 months. The patient reports that the pain is worse in the morning and typically resolves within a few hours. The patient is otherwise healthy and denies headache, visual disturbances, or difficulty chewing. Physical examination does not demonstrate swelling and normal range of motion is noted at all joints. Palpation of the scalp arteries fails to elicit tenderness. Laboratory results reveal the following.

|                                |                         |
|--------------------------------|-------------------------|
| Leukocyte count                | 8,000/mm <sup>3</sup>   |
| Hemoglobin                     | 12.4 g/dL               |
| Platelets                      | 380,000/mm <sup>3</sup> |
| Erythrocyte sedimentation rate | 92 mm/h                 |
| TSH                            | 2.1 $\mu$ U/mL          |

Which of the following is the best next step in management for this patient's condition?

- (A) High-dose corticosteroids
- (B) Low-dose corticosteroids
- (C) Temporal artery biopsy
- (D) Nonsteroidal anti-inflammatory drugs (NSAIDs)

**The answer is B: Low-dose corticosteroids.** The patient in this question is presenting with signs and symptoms consistent with a diagnosis of polymyalgia rheumatica (PMR), including chronic pain in the shoulders and hips, morning stiffness, elevated ESR, and age greater than 50. Of note, the physical examination in PMR is usually insignificant and the range of motion is typically normal without any associated tenderness or pain. The treatment of choice for PMR is low-dose prednisone. PMR can be associated with temporal arteritis (also known as giant cell arteritis). (A, C) Symptoms of temporal arteritis include headache, vision loss, tenderness over the temporal artery, and jaw claudication. Since the patient denies these symptoms, temporal arteritis is highly unlikely; therefore, temporal artery biopsy is unnecessary at this time. The treatment for temporal arteritis is immediate high-dose corticosteroids in order to prevent blindness. (D) NSAIDs are helpful in PMR for mild pain or while patients are being tapered off of corticosteroids. However, they are not the first choice in management as they are not as effective as corticosteroids.

3

A 28-year-old man with a history of asthma presents with worsening lower back pain. He describes the pain as constantly aching and deep. The pain is exacerbated with movement, but not relieved entirely by rest. He is unable to recall any inciting event. Review of systems is otherwise unremarkable. The patient refuses to give a social history. The patient has a temperature of 37°C, blood pressure of 120/80 mmHg, and heart rate of 76 beats per minute. On physical examination, there is exquisite tenderness to gentle percussion over the lumbar vertebral spinous processes. A straight leg test is performed and is normal. Laboratory results are within normal limits except for a significantly elevated erythrocyte sedimentation rate (ESR) of 240 mm/h.

Which of the following is the most likely diagnosis in this patient?

- (A) Prostate cancer
- (B) Ankylosing spondylitis
- (C) Vertebral osteomyelitis
- (D) Disk herniation

**The answer is C: Vertebral osteomyelitis.** This patient is presenting with signs and symptoms of vertebral osteomyelitis. The most common pathogen involved in vertebral osteomyelitis is *S. aureus* and those at risk include IV drug users, sickle cell patients, and immunosuppressed patients. Of note, the physical examination is critical in diagnosing vertebral osteomyelitis as tenderness to gentle percussion over the spinous process of the involved vertebrae is a specific finding. ESR is often elevated in vertebral osteomyelitis. The best initial step in management when vertebral osteomyelitis is suspected is to order an MRI as this is the most sensitive study. Treatment includes long-term IV antibiotics.

(A) This patient is quite young to have prostate cancer. Furthermore, the patient does not endorse any systemic symptoms. The localized pain on palpation is not characteristic of metastatic prostate cancer. (B) Ankylosing spondylitis often occurs in young men, but is characterized by pain and limited range of lower back motion. Symptoms are worse in the morning and localized tenderness to palpation at the vertebrae is not usually present. (D) Disk herniation is highly unlikely given the negative straight leg test and lack of recall of an inciting traumatic event. Also, tenderness to palpation is less likely over the spinous processes in the setting of a disk herniation.

4

A 46-year-old obese woman with a history of type 2 diabetes mellitus presents with severe left-sided foot pain for the last 6 weeks. The patient has had much difficulty ambulating and has to use a wheelchair now due to the pain. Physical examination demonstrates a severely deformed left foot and x-rays confirm extra-articular bone fragments, varying sizes of osteophytes, and several effusions in the small joints of the left foot.

Which of the following is the underlying mechanism of this patient's disease?

- (A) Avascular necrosis
- (B) Nerve damage
- (C) Uric acid deposition
- (D) Autoimmune destruction

**The answer is B: Nerve damage.** This patient is presenting with Charcot joint (neurogenic arthropathy) secondary to diabetic neuropathy. Charcot joint first develops from an inability to detect pain, proprioception, and temperature, which is likely the end result of years of peripheral nerve damage from diabetes. Over time, patients get secondary joint disease and deformation by traumatizing weight-bearing joints. X-ray is diagnostic and reveals osteophytes, loose bone fragments, and cartilage loss. Treatment includes managing the underlying diabetes and offering special shoes for mechanical support and to reduce further trauma. (A) Avascular necrosis (AVN) causes bone destruction from poor *vascular* supply (not neuropathically mediated). AVN can occur with corticosteroid use, trauma, and autoimmune disease. (C) Uric acid deposition causes gout. It usually affects the big toes and ankles and is severely painful. (D) Charcot joint is not the result of an autoimmune process such as rheumatoid arthritis.

5

A 43-year-old woman presents with chronic pain that she describes as occurring “all over her body.” Any movement exacerbates the pain and she reports much difficulty falling asleep at night. She constantly feels fatigued, but she denies fever, weight loss, or obvious muscle weakness. The patient has tried acetaminophen to no avail and has even attempted to run 1 to 2 miles per day with no improvement in her symptoms. The patient has an insignificant past medical history. Physical examination is significant for tenderness to palpation over several specific locations on her body. Neurologic examination is unremarkable and laboratory results are all within normal limits.

Given this patient's most likely diagnosis, which of the following is the best initial treatment?

- (A) Prednisone
- (B) Naproxen
- (C) Amitriptyline
- (D) Colchicine

**The answer is C: Amitriptyline.** The patient in this question is presenting with signs and symptoms consistent with a diagnosis of fibromyalgia (FM). FM is more common in middle-aged women and is characterized by chronic widespread pain and allodynia (a heightened and painful response to pressure). Physical examination is typically normal except for point muscle

tenderness in several areas including the mid-trapezius, lateral epicondyle, and greater trochanter, among others. Of note, FM has no laboratory findings that are diagnostic of the condition. The first-line treatment for FM is patient education, aerobic exercise, and good sleep hygiene. This patient has clearly attempted those recommendations based on the history she provides, so the first-line *medication* is a tricyclic antidepressant (TCA) such as amitriptyline. Several other drugs (pregabalin and duloxetine) can be attempted if TCAs fail to alleviate the patient's symptoms. **(A, B)** Corticosteroids and NSAIDs are useful in treating *inflammatory* conditions, but FM is not an inflammatory condition (not associated with elevated inflammatory markers such as ESR). **(D)** Colchicine is useful in treating gout, not FM.



A 27-year-old man presents with worsening low back pain over the past 5 months. He reports that the pain is most severe in the morning and describes a “back stiffness” when getting out of bed. He reports moderate improvement with walking. The patient denies any systemic symptoms and reports an insignificant past medical history. On physical examination, the patient is afebrile with normal vital signs. On musculoskeletal examination, there is marked tenderness over the sacroiliac joints with limited range of motion on forward flexion of the lower back.

Of the following tests, which is the best test for the likely diagnosis in this patient?

- (A)** MRI of the spine
- (B)** HLA-B27 serologic testing
- (C)** Plain film x-ray of the sacroiliac joints
- (D)** Rheumatoid factor testing

**The answer is C: Plain film x-ray of the sacroiliac joints.** The patient in this question is presenting with signs and symptoms consistent with ankylosing spondylitis (AS). AS is one of the seronegative spondyloarthropathies, which are joint diseases affecting the vertebral column that are characterized by a negative rheumatoid factor (RF) and ANA. AS is more common in men, typically occurs in the second and third decades of life, and is characterized by progressive low back pain and stiffness lasting at least 3 months in duration. Morning stiffness and improvement with exercise are also common with this condition. In order to *confirm* the diagnosis, anteroposterior (AP) x-ray of the sacroiliac (SI) joints is performed. Fusion of the SI joints (the presence of a “bamboo spine”) is diagnostic and a specific indicator for the diagnosis of AS.

**(A)** MRI of the spine would only be necessary if the x-ray of the lumbar spine returns negative and AS is clinically suggested. **(B)** Although patients with AS have an increased incidence of positivity for HLA-B27 (90% of patients), it is not a *specific* test because only a minority of patients demonstrating positivity for HLA-B27 actually has AS. **(D)** AS is a *seronegative* spondyloarthropathy, so by definition it is negative for RF levels.

7 A 47-year-old woman who has not seen a physician in over 20 years presents with painful joints, fatigue, weakness, and what she describes as “hideously misshapen hands.” Family history is significant for type 1 diabetes. Physical examination reveals deformed hands and a 2-cm soft mass that is mobile and tender to palpation in the left popliteal fossa.

Which of the following is the underlying pathophysiology of this popliteal fossa mass?

- (A) Monosodium urate crystal deposition
- (B) Redundant bone growth
- (C) Obstruction of lymphatic drainage
- (D) Fluid production from inflamed synovium

**The answer is D: Fluid production from inflamed synovium.** This patient is presenting with signs and systemic symptoms consistent with rheumatoid arthritis (RA). The tender mass in the popliteal fossa is likely a Baker cyst, a benign swelling of the synovial bursa found behind the knee joint. Baker cysts are caused by excessive fluid production from the inflamed synovium that commonly occurs in rheumatoid arthritis, a systemic inflammatory disorder that primarily attacks synovial joints. (A) Urate crystal deposition is a finding in gout, but this would cause the knee to be painful, erythematous, and swollen. Furthermore, it would be highly unusual for the swelling seen in a gouty knee flare to be limited to the popliteal fossa. (B) Redundant bone growth would not be tender and soft on physical examination. Such bone growth can be seen as osteophytes in osteoarthritis. (C) Obstruction of lymphatic drainage causes lymphedema, which is highly unlikely to occur in the popliteal fossa.

8 A 47-year-old obese man presents with pain in his bilateral knees that has worsened over the last year. The pain is alleviated by rest and worsened by walking. The patient has never taken any medications for the pain, but warm compresses temporarily cause relief. The patient has a history of type 2 diabetes and hyperlipidemia. Physical examination shows a BMI of 33 kg/m<sup>2</sup>. A “grating” sound is appreciated on palpation over the knee joints bilaterally.

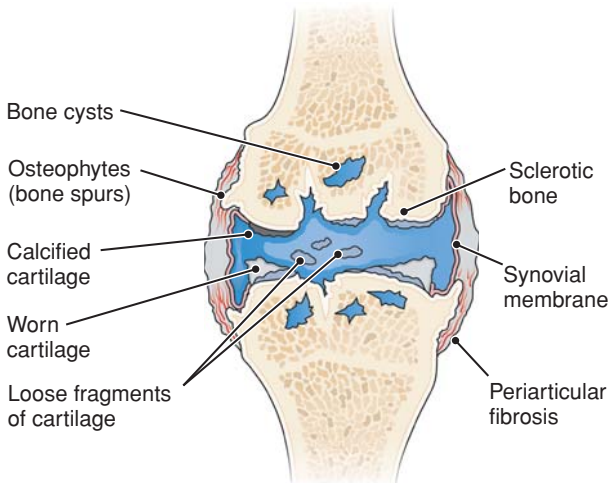
Which of the following is the best initial treatment for this patient?

- (A) Intra-articular corticosteroid injection
- (B) Acetaminophen
- (C) Naproxen
- (D) Allopurinol

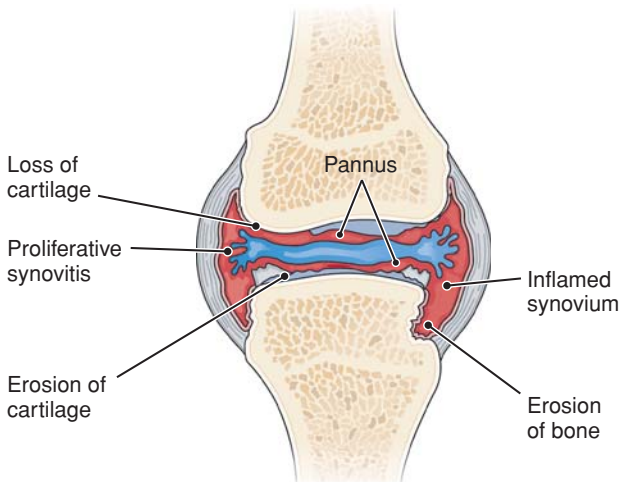
**The answer is B: Acetaminophen.** This patient is obese, greater than 40 years of age, and is presenting with bilateral knee pain. The fact that the pain is worsened with activity and relieved by rest suggests that it is most likely secondary to osteoarthritis (OA). If he reported morning stiffness lasting greater than 30 minutes and had systemic symptoms, rheumatoid arthritis would have been the likely diagnosis. OA is a *noninflammatory* arthritis that results in eroding



cartilage in the intra-articular joints. This causes joint crepitus (a “grating” or popping sound) that occurs when the surfaces of the joint grind against each other. Although the diagnosis is usually made clinically, the typical changes seen on x-ray include joint space narrowing, subchondral sclerosis (increased bone formation around the joint), subchondral cyst formation, and osteophytes (Figure 9-4 shows the articular changes seen in osteoarthritis and rheumatoid arthritis)



**A** Advanced osteoarthritis



**B** Rheumatoid arthritis

**Figure 9-4**

arthritis). Acetaminophen is the first-line treatment for mild to moderate OA. It is just as efficacious as NSAIDs in alleviating the pain in OA with considerably fewer side effects. Nonetheless, while most guidelines do indeed recommend acetaminophen as first-line treatment for pain, acetaminophen toxicity remains a real public health concern as it is the leading cause of acute liver failure in the United States. The therapeutic window of acetaminophen is not wide; in fact, toxicity occurs just above the recommended 4 g/d for adults.

(A) Intra-articular corticosteroid injections lead to short-term pain relief that lasts up to a few months. This should not be the initial treatment in OA. (C) Naproxen is an NSAID and although NSAIDs have been shown to be efficacious in the treatment of OA, their side effect profile consists of gastrointestinal and renal consequences that make them second-line treatments. (D) Allopurinol is used in the prophylactic treatment of gout. It acts via inhibition of xanthine oxidase, which decreases production of uric acid. It is not used in the treatment of OA.



A 53-year-old woman presents with a 2-week history of fatigue and weakness in her hips. She has also started developing weakness in her shoulders while trying to brush her hair in the mornings. The patient denies any difficulty chewing, blurry vision, or facial weakness. The patient is otherwise healthy and does not report any family history other than pancreatic cancer in her maternal uncle. Neurologic examination reveals 3/5 strength in the proximal muscles of her upper and lower extremities. The patient's erythrocyte sedimentation rate (ESR) is elevated at 92 mm/h and the creatine kinase (CK) is moderately elevated. Other laboratory values (including TSH and free T4) are within normal limits.

Which of the following is the most likely diagnosis in this patient?

- (A) Amyotrophic lateral sclerosis (ALS)
- (B) Polymyositis
- (C) Drug-induced myopathy
- (D) Fibromyalgia

**The answer is B: Polymyositis.** The patient in this question is presenting with signs, symptoms, and laboratory values consistent with a diagnosis of polymyositis, an inflammatory myopathy characterized by proximal muscle weakness. Dysphagia and esophageal dysmotility occur in as many as one-third of patients. It typically occurs between 40 and 50 years of age and women are more commonly affected. The elevation in ESR and CK levels support the diagnosis of an inflammatory myopathy. Polymyositis can be confirmed by electromyography (EMG) and positive muscle biopsy. It is treated with corticosteroids. (A) ALS presents with weakness as well, but it is associated with upper *and* lower motor neuron deficits. (C) Drug-induced myopathy (commonly caused by alcohol, antipsychotic medications, and statins) would

present clinically with similar symptoms, but would not have an elevated ESR and CK. (D) Fibromyalgia typically presents with *pain*, not objective weakness, and would have normal ESR and CK levels.

**10** A 67-year-old woman presents with severe headaches, joint pain, painful chewing, and fever. On physical examination, prominent vasculature is noted in the temporal region of the scalp. Decreased pulses are noted throughout the body. Laboratory testing reveals an ESR of 94 mm/h.

Which of the following is associated with this condition?

- (A) Aortic aneurysm
- (B) Inflammatory bowel disease
- (C) Hepatitis B
- (D) Smoking history

**The answer is A: Aortic aneurysm.** The patient in this question is presenting with signs, symptoms, and laboratory values consistent with a diagnosis of giant-cell arteritis (GCA), also known as temporal arteritis. Symptoms can include headache, visual problems, jaw claudication, fever, and temporal scalp tenderness. GCA is a vasculitis most commonly involving large and medium arteries of the head, predominantly the branches of the external carotid artery. A decreased temporal artery pulse can be noted as well. ESR and C-reactive protein are commonly elevated. High-dose corticosteroids should be started as soon as the diagnosis is suspected (even before confirmation by biopsy) to prevent irreversible blindness secondary to ophthalmic artery occlusion. GCA can involve branches of the aorta leading to aortic aneurysm, thus patients should have serial chest x-rays performed.

(B) Inflammatory bowel disease includes ulcerative colitis and Crohn disease and is not associated with GCA. (C) Hepatitis B is associated with polyarteritis nodosa (30% of the time), a vasculitis of medium- and small-sized arteries. (D) A smoking history is seen in thromboangiitis obliterans (Buerger disease), which presents with progressive inflammation and thrombosis of small and medium arteries of the hands and feet. Ulceration and gangrene are common complications.

**11** A 27-year-old man presents with 6 months of worsening low back pain. The pain is worse in the morning and associated with morning “stiffness” that improves with walking and exercise. The patient feels well and denies any systemic symptoms. Physical examination reveals limited range of motion on forward flexion of her lower back. X-ray reveals the presence of a “bamboo spine.”

Which of the following is the most common extra-articular manifestation of this patient's condition?

- (A) Aortic valve insufficiency
- (B) Lung fibrosis
- (C) Anterior uveitis
- (D) Oral ulcers

**The answer is C: Anterior uveitis.** The patient in this question is presenting with signs, symptoms, and radiologic findings consistent with a diagnosis of ankylosing spondylitis (AS). AS has a strong association with HLA-B27. The most common extra-articular manifestation of AS is anterior uveitis: inflammation in the anterior chamber of the eye. This can cause erythema, pain, and photophobia. The reason for this association is that both AS and uveitis share an inheritance with the HLA-B27 antigen. (A, B) Both aortic valve insufficiency and lung fibrosis are less commonly associated with AS. (D) Oral ulcers are associated with systemic lupus erythematosus (SLE) and Crohn disease, but not associated with AS.

**12** A 37-year-old woman with a history of Crohn disease presents for follow-up. She has been taking prednisone for the last 4 years at varying dosages and now has worsening left hip pain. The pain is aggravated during weight-bearing activities and is not relieved by rest. Physical examination is significant for a blood pressure of 148/82 mmHg and limited range of motion of her left hip. Dermatologic examination reveals purple striae and thinning of her skin in the lower abdominal region. Neurologic examination is within normal limits. Laboratory values (including ESR and TSH) are within normal limits.

Which of the following is the underlying mechanism of this patient's left hip pain?

- (A) Cartilage erosion
- (B) Interruption of bone vasculature
- (C) Excessive fluid production from inflamed synovium
- (D) Peripheral nerve damage

**The answer is B: Interruption of bone vasculature.** This patient is steroid-dependent and is presenting with signs and symptoms consistent with a diagnosis of avascular necrosis, also known as osteonecrosis. This condition results when there is necrosis of bone components due to interruption of the blood supply. Avascular necrosis manifests with progressive pain with a limited range of motion. Risk factors include chronic corticosteroid use, alcoholism, hemoglobinopathies (e.g., sickle cell disease), HIV, and chemotherapy. The best and most sensitive test for avascular necrosis is MRI. (A) Cartilage erosion occurs in osteoarthritis. (C) Excessive fluid production from inflamed

synovium describes an inflammatory arthritis such as rheumatoid arthritis. (D) Peripheral nerve damage can occur in diabetic patients and results in Charcot joint, which manifests as a deformed foot that develops from an inability to detect pain, proprioception, and temperature.

13

A 37-year-old woman presents with progressive shortness of breath. The patient also reports painful joints over the past 5 months, especially in her fingers. She has a past medical history of GERD, which is controlled with omeprazole. On physical examination, the patient has thickened skin over the acral surfaces. Examination reveals the following (*Figure 9-5*).



**Figure 9-5**

Which of the following will likely be positive in this patient?

- (A) Anti-histone antibodies
- (B) RF
- (C) Anti-topoisomerase antibodies
- (D) Cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA)

**The answer is C: Anti-topoisomerase antibodies.** This patient likely has a diagnosis of systemic sclerosis, an autoimmune and connective tissue disease that is characterized by thickening of the skin from accumulation of collagen. There are two forms of systemic sclerosis: limited cutaneous scleroderma (i.e., CREST syndrome, which is limited to the skin on the face, hands, and feet) and diffuse cutaneous scleroderma (covers more of the skin and commonly involves the visceral organs such as the kidneys, heart, lungs, and gastrointestinal tract). Importantly, “CREST” refers to the five main features: Calcinosis, Raynaud phenomenon, Esophageal dysmotility, Sclerodactyly, and

Telangiectasia. CREST syndrome is characterized by the presence of anti-centromere antibodies. Our patient is presenting with lung findings and therefore likely has the *diffuse* form of systemic sclerosis. This condition is characterized by the presence of anti Scl-70 antibodies (also called *anti-topoisomerase I* antibodies).

(A) Anti-histone antibodies are found in drug-induced lupus. Medications that are most likely responsible include hydralazine, procainamide, and isoniazid. (B) Rheumatoid factor (RF) is often found in rheumatoid arthritis but can also be found in a plethora of other autoimmune diseases. (D) Positive c-ANCA is found in granulomatosis with polyangiitis (Wegener granulomatosis).



A 47-year-old woman presents with diffuse joint pain over the past 5 days. Although the pain is diffuse, it is worst in the hand and wrist joints. The pain is at its worst in the morning and typically can take up to 20 minutes to reach the point where she can actually perform activities like walking and writing. The patient is otherwise healthy and denies fever, chills, weight loss, fatigue, or skin rashes. The patient reports that she is a third-grade teacher and has had several sick students over the past 4 months. Physical examination is unremarkable and no swelling or redness is noted over her joints. Laboratory values reveal a hemoglobin of 13.5 g/dL and an ESR of 18 mm/h.

Which of the following is the likely diagnosis in this patient?

- (A) Fibromyalgia
- (B) Rheumatoid arthritis
- (C) Polymyalgia rheumatica
- (D) Symmetric arthritis secondary to a viral infection

**The answer is D: Symmetric arthritis secondary to a viral infection.** The patient in this question likely has viral arthritis from parvovirus B19 infection. Viral arthritis is distinguished from other types of arthritis by its acute onset of *symmetric* and *polyarticular* symptoms. Furthermore, it typically resolves entirely within 2 months and does not cause elevated inflammatory laboratory values (such as ESR). Our patient has only had symptoms for 5 days. The fact that she is in contact with children on a daily basis is a clue to the diagnosis as well. Although children typically present with the “slapped cheek” rash when infected by parvovirus B19, adults usually present with arthralgias typically affecting the finger and wrist joints.

(A) The diagnosis of fibromyalgia relies on tenderness in at least 11 out of the 18 “trigger” sites. (B) Rheumatoid arthritis (RA) is an inflammatory arthritis and would likely have an elevated ESR. Furthermore, RA typically presents with swelling, systemic symptoms, and morning stiffness lasting *greater* than 30 minutes. (C) Polymyalgia rheumatica presents with pain and/or stiffness in the shoulders and hips of an older patient. Moreover, the diagnosis is made only with a highly elevated ESR.

- 15** A 53-year-old man with a history of systemic lupus erythematosus (SLE) presents with hematuria. A renal biopsy demonstrates proliferative glomerulonephritis and the patient is started on cyclophosphamide.

Which of the following conditions is this patient at risk for developing with the initiation of this medication?

- (A) Peripheral neuropathy
- (B) Hearing loss
- (C) Hemorrhagic cystitis
- (D) Thyroid abnormalities

**The answer is C: Hemorrhagic cystitis.** Cyclophosphamide is a nitrogen mustard alkylating agent used to treat cancers and autoimmune disorders such as SLE and the vasculitides. With respect to SLE, cyclophosphamide is used primarily in patients with renal pathology. Side effects of cyclophosphamide include hemorrhagic cystitis, bladder cancer, and myelosuppression. Fortunately, patients can be administered mesna and encouraged to drink liberal amounts of fluids to prevent these complications. (A) Peripheral neuropathy is a toxic side effect of vincristine use. Other causes of peripheral neuropathy include phenytoin, alcohol, isoniazid, and antiretroviral therapy. (B) Hearing loss, specifically cochlear dysfunction, can be seen with cisplatin and carboplatin. Other causes of hearing loss include aminoglycosides. (D) Thyroid abnormalities can be seen with amiodarone (useful both in supraventricular arrhythmias and ventricular arrhythmias) as well as lithium (useful in the prophylactic treatment of bipolar disorder).

- 16** A 29-year-old man who recently completed a course of antibiotics for nongonococcal urethritis secondary to *Chlamydia trachomatis* presents with diffuse joint pain. The patient describes the pain as particularly bothersome in his low back and left knee. The patient is otherwise healthy and has no other complaints. Physical examination reveals an afebrile man with normal vital signs. The patient's left knee is markedly swollen, erythematous, and exquisitely tender to palpation. Head and neck examination reveals bilateral redness in the eyes with epiphora. Joint aspiration is performed which reveals a leukocyte count of  $11,000/\text{mm}^3$ . Synovial fluid analysis also reveals a predominance of polymorphonuclear leukocytes.

Which of the following is associated with this patient's condition?

- (A) Chronic hyperuricemia
- (B) HLA-B27
- (C) Articular cartilage degradation
- (D) Inflammation of the synovium

**The answer is B: HLA-B27.** This patient is presenting with the classic triad found in reactive arthritis (Reiter syndrome), including nongonococcal

urethritis, arthritis, and conjunctivitis (best remembered by the phrase “*can’t see, can’t pee, can’t climb a tree*”). Reactive arthritis is a seronegative spondyloarthropathy, referring to the fact that it is negative for rheumatoid factor (RF). Think “PAIR” (Psoriatic arthritis, Ankylosing spondylitis, Inflammatory bowel disease, and Reactive arthritis) for remembering the seronegative spondyloarthropathies. These diseases are associated with an increased incidence of HLA-B27. (A) Chronic hyperuricemia can be seen in chronic gout and is best treated with allopurinol. (C) Articular cartilage degradation is seen in osteoarthritis. (D) Inflammation of the synovium is seen in rheumatoid arthritis.



A 39-year-old woman with a history of rheumatoid arthritis presents for routine care. The patient’s symptoms are well controlled on her current medication regimen. Routine laboratory values reveal the following.

|                               |                         |
|-------------------------------|-------------------------|
| Hemoglobin                    | 9.8 g/dL                |
| Mean corpuscular volume (MCV) | 110 fL                  |
| Leukocyte count               | 9,500/mm <sup>3</sup>   |
| Platelets                     | 280,000/mm <sup>3</sup> |

Which of the following is this patient taking for her rheumatoid arthritis?

- (A) Methotrexate
- (B) Cyclosporine
- (C) Corticosteroids
- (D) Hydroxychloroquine

**The answer is A: Methotrexate.** The patient in this question has rheumatoid arthritis and is presenting with a macrocytic anemia (MCV >100 fL). Of the four choices, only methotrexate can cause a macrocytic anemia. Methotrexate is a disease-modifying antirheumatic drug (DMARD), which inhibits the metabolism of folic acid by inhibiting dihydrofolate reductase. Other important side effects include stomatitis, lung fibrosis, rash, and pancytopenia. Therefore, patients on methotrexate need to have their blood counts (CBC) checked every 3 months. (B) Cyclosporine is an immunosuppressant drug used commonly after organ transplantation. It is associated with increased viral infection, nephrotoxicity, hypomagnesemia, and hepatotoxicity. (C) Corticosteroids are used in the treatment of rheumatoid arthritis (RA) and side effects include osteoporosis, impaired wound healing, and other effects seen in Cushing syndrome. (D) Hydroxychloroquine is also a DMARD used in the treatment of RA, but its side effects include visual problems and hemolytic anemia found in G6PD deficiency.



18

A 4-year old boy presents with fever, swollen lymph nodes, and headache for the past 3 days. Physical examination demonstrates a fever of  $38.4^{\circ}\text{C}$  and a heart rate of 110 beats per minute. There is conjunctival injection, bilateral swelling of the anterior cervical lymph nodes, and a morbilliform rash over the upper and lower extremities. Oral examination reveals a diffusely red and enlarged tongue.

Which of the following is likely to develop if this condition goes untreated?

- (A) Leukemia
- (B) Blindness
- (C) Coronary artery aneurysm
- (D) Pulmonary embolism

**The answer is C: Coronary artery aneurysm.** This patient is presenting with an autoimmune disorder called Kawasaki disease, also known as mucocutaneous lymph node syndrome. This is a large- and medium-sized vessel vasculitis mostly seen in children under the age of 5. It affects many organ systems including the blood vessels, skin, mucous membranes, and lymph nodes. The most rare but serious effect is on the heart, where it can cause fatal coronary artery aneurysms in untreated children. Unlike Wegener granulomatosis, microscopic polyangiitis, and Churg–Strauss syndrome, Kawasaki disease is *not* associated with ANCA antibodies. The diagnosis of Kawasaki disease relies on the presence of fever for at least 5 days in addition to four out of five of the following criteria (known as *CRASH*): Conjunctivitis (bilateral), Rash (usually trunk), Aneurysms (coronary), Strawberry tongue, and/or Hand and feet erythema. Cervical lymphadenopathy can also be added to this list. Treatment consists of intravenous immunoglobulin (IVIG, for prevention of coronary vasculitis) and high-dose aspirin (which is usually avoided in children due to Reye syndrome). Early treatment is critical to avoid the risk of coronary aneurysm.

(A) Kawasaki disease typically shows normocytic anemia and thrombocytosis; it does not result in leukemia. (B) Blindness is a complication of another large-vessel vasculitis called giant cell (or temporal) arteritis. (D) Kawasaki disease is not associated with the development of pulmonary embolism or pro-coagulative states.

19

A 32-year-old man of Turkish descent presents with painful oral and genital ulcers. He reports two previous episodes of oral ulcers that resolved within 2 weeks. The patient also reports blurred vision, diarrhea, and a cough. Physical examination reveals nonscarring oral mucocutaneous aphthous ulcerations and several discrete ulcerations on the shaft of the penis. The rest of the dermatologic examination reveals several hyperpigmented nodules on the bilateral anterior legs that are painful to palpation.

Which of the following is the most likely diagnosis in this patient?

- (A) Behçet disease
- (B) Herpes simplex virus (HSV) infection
- (C) Systemic lupus erythematosus (SLE)
- (D) Sarcoidosis

**The answer is A: Behçet disease.** This patient is presenting with recurrent oral ulcers, genital ulcers, blurred vision (likely secondary to anterior uveitis), erythema nodosum on the anterior legs, and diarrhea. Given this constellation of symptoms in combination with his Turkish descent, he likely has Behçet disease. This disease is a rare immune-mediated systemic vasculitis that often presents with mucous membrane ulceration and ocular problems. The triad that is often tested is recurrent oral aphthous ulcers, genital ulcers, and uveitis. This syndrome is much more common in Turkish, Central Asian, and Middle Eastern communities (commonly called the “Silk Road Disease” based on the old silk trading routes in the Middle East and Central Asia). The official diagnosis occurs when recurrent oral ulcers are present *with* two additional findings from the following: recurrent genital ulcers, either anterior uveitis or posterior uveitis, skin findings (papulopustular lesions, folliculitis, erythema nodosum, or acne in postadolescents not on corticosteroids), and/or positive pathergy test (papule >2 mm in diameter 24 to 48 hours or more after needle-prick).

(B) HSV infection results in small grouped vesicles on an erythematous base. This patient has *aphthous* ulcers, not herpetic vesicular lesions. (C) Systemic lupus erythematosus (SLE) results in oral ulcers, but is also associated with arthritis, hematologic abnormalities, malar rash, and other findings not seen in this patient. (D) Sarcoidosis can cause erythema nodosum (as seen on dermatologic examination in this patient) and cough; however, it also presents with dyspnea and sometimes chest pain. Ulcerations are not seen in sarcoidosis.

20

A 61-year-old man with a history of chronic alcoholism and parathyroid adenoma presents with pain in his left knee for the last 2 days. He denies fevers, chills, night sweats, or any history of trauma to the knee, but does endorse abdominal pain and constipation. Physical examination is significant for tenderness and erythematous skin overlying the left knee. There is also marked swelling of the left knee. Laboratory findings reveal an elevated calcium level (12.1 mg/dL).

If joint aspiration is performed, which of the following will be seen on synovial fluid analysis?

- (A) Negatively birefringent needle-shaped crystals
- (B) Positively birefringent rhomboid-shaped crystals
- (C) Neutrophil predominance with gram-positive cocci
- (D) Normal synovial fluid findings

**The answer is B: Positively birefringent rhomboid-shaped crystals.**

This patient has a history of parathyroid adenoma that is likely causing hypercalcemia secondary to hyperparathyroidism. Patients with hypercalcemia are at risk for developing pseudogout, a rheumatologic disease with diverse symptoms and signs arising from the accumulation of calcium pyrophosphate dihydrate crystals in the connective tissues. It commonly presents with acute onset, painful monoarthropathy of the knee. Joint aspiration with synovial fluid analysis confirms the diagnosis, showing rhomboid-shaped crystals that are positively birefringent. (A) Negatively birefringent needle-shaped crystals describe *gout*, which also presents with acute onset monoarthropathy, but usually affects the first metatarsophalangeal joint of the foot. Furthermore, gout is not triggered by hypercalcemia. (C) Neutrophil predominant synovial fluid with gram-positive cocci is diagnostic of septic arthritis. This patient has no fever, making septic arthritis highly unlikely from the clinical picture alone. (D) Normal synovial fluid findings are not the norm in the setting of pseudogout.

**21** A 60-year-old woman presents with vision loss in her left eye and worsening headache. The patient has had a “baseline” headache on the left side for the last 3 months, but it has worsened over the past few days. Her past medical history is significant for diabetes, hyperlipidemia, and hypertension. She has a temperature of 37°C, blood pressure of 148/76 mmHg, and heart rate of 76 beats per minute. Physical examination reveals complete loss of vision in her left eye. Laboratory values reveal an ESR of 82 mm/h.

Which of the following is the best next step in management of this patient’s condition?

- (A) Temporal artery biopsy
- (B) Low-dose corticosteroids
- (C) Sumatriptan and supplemental oxygen
- (D) High-dose corticosteroids

**The answer is D: High-dose corticosteroids.** This patient is presenting with signs, symptoms, and laboratory values consistent with a diagnosis of giant cell arteritis (GCA), also known as temporal arteritis. This is a chronic vasculitis of medium and large vessels that often presents with loss of vision, headaches, and an elevated ESR. Physical examination sometimes reveals diminished pulses and abnormal fundoscopic findings. In order to prevent permanent blindness, a patient with suspected GCA should immediately undergo treatment with high-dose intravenous methylprednisolone as up to 50% of untreated patients will go on to develop blindness. (B) Low-dose oral corticosteroids would be given as a taper over several months *following* administration of high-dose corticosteroids in the acute setting of GCA. (A) Temporal artery biopsy is certainly indicated here in order to *confirm* the diagnosis

of GCA. However, therapy should not be delayed while waiting for results of the biopsy. (C) Sumatriptan and supplemental oxygen would be indicated in the setting of acute migraine or cluster headache. This patient has a headache, but her associated symptoms and elevated ESR make GCA the likely diagnosis.

22

A 37-year-old man presents with low back pain. He also endorses morning stiffness of his lower back. Both the pain and the stiffness improve with exercise. The patient has also noted bloody diarrhea over the past 2 weeks, but his friend told him that since he often weight-lifts, it is most likely secondary to hemorrhoids. Physical examination reveals pain on palpation over the sacroiliac joints. Dermatologic examination confirms several discrete violaceous nodules that are painful to palpation over the bilateral shins. Fecal occult blood test is positive and laboratory values reveal a hemoglobin level of 10.1 g/dL and high p-ANCA titers.

Which of the following is the most likely underlying disease contributing to this patient's symptoms?

- (A) Celiac disease
- (B) Reactive arthritis
- (C) Ulcerative colitis
- (D) *Giardia lamblia*

**The answer is C: Ulcerative colitis.** This patient is presenting with signs and symptoms consistent with an underlying inflammatory bowel disease (IBD), most likely ulcerative colitis. The acute onset of bloody diarrhea in combination with anemia and positive fecal occult blood testing in the setting of his relatively young age lend credence to the diagnosis. This patient is also demonstrating extraintestinal manifestations of ulcerative colitis, including erythema nodosum and arthritis (similar in presentation to ankylosis spondylitis). p-ANCA is positive in high titers in ulcerative colitis, as seen with this patient. (A) Celiac disease is an autoimmune disease typified by malabsorption. Testing reveals anti-endomysial antibodies and anti-transglutaminase antibodies. Skin findings include dermatitis herpetiformis. (B) Reactive arthritis is characterized by nongonococcal urethritis, conjunctivitis, and arthritis. (D) *Giardia lamblia* infection causes a foul-smelling steatorrhea secondary to malabsorption. Bloody diarrhea is not present.

## Dermatology

1

A 62-year-old man with an insignificant past medical history presents with anxiety about several “skin bumps.” He has a family history of melanoma and endorses spending much time in the sun as a child. Physical examination is unremarkable except for the lesion seen in the figure below (*Figure 10-1*).



**Figure 10-1**

Which of the following represents the most appropriate next step in management?

- (A) Shave biopsy
- (B) Reassurance
- (C) Excisional biopsy
- (D) Topical corticosteroids

**The answer is B: Reassurance.** The patient in this question is presenting with skin lesions that have a “stuck on” appearance with an overlying rough and scaly surface. This is a classic example of the common dermatologic condition known as seborrheic keratosis. Seborrheic keratoses are benign skin growths that require no treatment. (A, C) If there is doubt about the less common likelihood of nodular melanoma, a biopsy should be performed. Of note, the sudden appearance of many seborrheic keratoses can be a sign of a gastrointestinal malignancy.

---

2

A 22-year-old man with a history of asthma presents with a 2-day history of several small and scaling erythematous papules and plaques on his torso, back, and all four extremities. The patient reports that 3 weeks ago he had an unrelenting sore throat that just recently resolved. The patient has never had this skin condition before and denies a family history of psoriasis or any other dermatologic condition.

Which of the following is the likely diagnosis?

- (A) Plaque-like psoriasis
- (B) Pustular psoriasis
- (C) Guttate psoriasis
- (D) Erythrodermic psoriasis

**The answer is C: Guttate psoriasis.** The patient's clinical presentation in this question is consistent with a diagnosis of guttate psoriasis. Guttate psoriasis is the second most common form of psoriasis and accounts for less than 10% of cases. Dermatologic examination reveals numerous small and scaling erythematous papules and plaques on the torso and extremities. This type of psoriasis often follows streptococcal pharyngeal infection, so patients should be asked about a recent sore throat or diagnosis of streptococcal pharyngitis. (A) Plaque-like psoriasis is the most common form of psoriasis (nearly 90%) and is characterized by sharply demarcated erythematous scaling plaques, commonly on the elbows, knees, and scalp. (B, D) Pustular and erythrodermic psoriasis are the most severe forms of psoriasis as they both can compromise the protective functions of the skin (temperature control, fluid maintenance, electrolyte balance). Pustular psoriasis is associated with pus-filled blisters rather than plaques. Erythrodermic psoriasis, unlike the other types of psoriasis, usually affects the entire body and gives the skin a “burned” appearance.

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3

A 32-year-old woman presents with pruritic skin lesions on the upper back. The patient reports that the number of skin lesions has increased over the last 2 years. Physical examination reveals several hypopigmented macules of varying sizes affecting the upper back. Dermoscopy reveals fine scale over the majority of the lesions. A potassium hydroxide examination is performed (*Figure 10-2*).

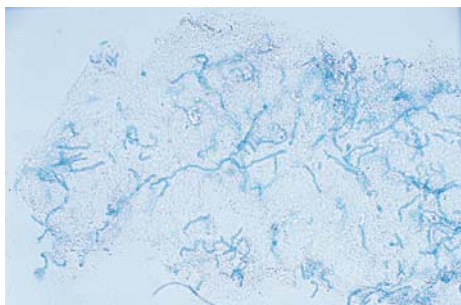


Figure 10-2

Which of the following is the correct treatment for this condition?

- (A) Topical corticosteroids
- (B) Terbinafine
- (C) Topical selenium sulfide
- (D) Reassurance

**The answer is C: Topical selenium sulfide.** The patient in this question likely has pityriasis (tinea) versicolor, a superficial fungal infection with *Malassezia* species. The skin lesions in pityriasis versicolor are hypopigmented or hyperpigmented macules of varying sizes, often affecting the upper trunk, arms, chest, shoulders, and face. The skin lesions in this condition are often irregular, well-demarcated, covered by a fine scale, and mildly pruritic. Given the interference with melanin production, pityriasis versicolor often results in hypopigmented lesions, but in light-skinned people, lesions can be pink or light brown. A potassium hydroxide examination is diagnostic and reveals a “spaghetti and meatballs” appearance (rod-shaped hyphae intermixed with spores). Treatment is with topical selenium sulfide or topical ketoconazole. (A) Topical corticosteroids would treat the symptomatic itching, but not the underlying fungal infection. (B) Terbinafine would indeed treat pityriasis versicolor, but is too strong of a medication (associated hepatotoxicity) to use as first-line therapy. This would be an appropriate agent if the patient does not respond to topical treatment. (D) Reassurance should not be offered as a treatment option due to the pruritus affecting an individual's quality of life.

4

A 42-year-old man presents with a chronic and severely pruritic rash on his bilateral elbows and buttocks. The patient first noticed the rash 9 months ago and reports that the itching has worsened over the last 3 months. Review of systems is unremarkable except for some loose stools over the past 3 years. Physical examination reveals grouped papulovesicular lesions on the extensor regions of his bilateral elbows and buttocks (Figure 10-3).



**Figure 10-3**

Which of the following diseases is associated with this chronic blistering skin condition?

- (A) Crohn disease
- (B) Celiac disease
- (C) Ulcerative colitis
- (D) Herpes simplex virus

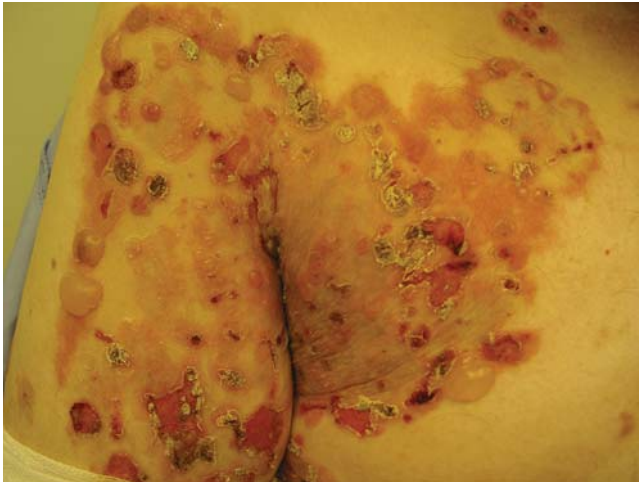
**The answer is B: Celiac disease.** The patient in this question likely has dermatitis herpetiformis, a chronic blistering skin condition characterized by intensely pruritic papulovesicular skin lesions located symmetrically on extensor surfaces. Although the mechanism is not fully known, dermatitis herpetiformis is associated with gluten intolerance and celiac disease. Diagnosis is confirmed by ordering anti-endomysial antibodies of the IgA type and a skin biopsy (immunofluorescent studies demonstrate IgA in the dermal papillae). Treatment is with a gluten-free diet and dapsone (mechanism of efficacy is not entirely understood). (A, C) Crohn disease and ulcerative colitis both can present with extraintestinal manifestations, but not dermatitis herpetiformis. Rather, ulcerative colitis and Crohn disease are associated with pyoderma gangrenosum (deep necrotic ulcers typically located in the lower extremities). (D) Although the name dermatitis herpetiformis seems to suggest a relationship with the herpes virus, the name is simply based on the skin lesions looking similar to herpetic lesions (grouped vesicles).



A 57-year-old man presents with a blistering rash on his chest and upper arm (*Figure 10-4*). He reports that the blisters often erupt and are mildly pruritic. He denies oral lesions. Nikolsky sign is negative.



Biopsy is performed which reveals linear immunofluorescence of the epidermal basement membrane.



**Figure 10-4**

Which of the following is the underlying mechanism of this disease?

- (A) IgG antibodies against desmosomes
- (B) Deposits of IgA at the tips of dermal papillae
- (C) Type IV hypersensitivity reaction following exposure to allergen
- (D) IgG antibodies against hemidesmosomes

**The answer is D: IgG antibodies against hemidesmosomes.** The patient in this question is presenting with signs and symptoms consistent with bullous pemphigoid. Given that Nikolsky sign (separation of the epidermis with lateral stroking of the skin) is negative and the biopsy demonstrated linear immunofluorescence of the epidermal basement membrane, bullous pemphigoid is more likely than pemphigus vulgaris. The underlying mechanism of this autoimmune disease involves IgG antibodies against hemidesmosomes (located on the epidermal basement membrane). Bullous pemphigoid often spares the oral mucosa and presents with tense blisters. (A) IgG antibodies against desmosomes is the mechanism underlying pemphigus vulgaris (PV), which has a higher mortality. Immunofluorescence studies in PV reveal antibodies around keratinocytes in a netlike pattern (intraepidermal separation rather than subepidermal separation associated with bullous pemphigoid). Furthermore, blisters tend to be flaccid in PV and Nikolsky sign is positive. (B) IgA deposition in the dermal papillae is the mechanism underlying dermatitis herpetiformis, which is associated with celiac disease. (C) A Type IV hypersensitivity reaction following exposure to an allergen is consistent with allergic contact dermatitis.

6

An 18-month-old infant presents with a diffuse rash that has worsened over the past 24 hours. His mother reports that he has been lethargic with a decreased appetite. The child is otherwise healthy, but did have symptoms consistent with an upper respiratory infection a few weeks prior to the onset of the rash. Physical examination reveals an afebrile infant with the following dermatologic finding (*Figure 10-5*).



**Figure 10-5**

Which of the following is the most common cause of this condition?

- (A) Drug reaction
- (B) Herpes simplex virus
- (C) *Mycoplasma pneumoniae*
- (D) Non-Hodgkin lymphoma

**The answer is B: Herpes simplex virus.** The patient in this question is presenting with pink-red papules and plaques with a pale central regions. The skin lesions have a “target” appearance, a classic description for erythema multiforme (EM). EM is a skin condition whose cause remains unclear but likely is secondary to immune complex deposition in superficial microvasculature of the skin. EM usually follows infection or drug exposure. The most common cause

of EM is herpes simplex virus (HSV). (A, C, D) Drug reactions (sulfa drugs, phenytoin,  $\beta$ -lactam antibiotics), *Mycoplasma pneumoniae*, and non-Hodgkin lymphoma are also causes of EM, but not as common as HSV infection.

7

A 77-year-old man presents with a rough bump on his left ear. It is sometimes pruritic, but otherwise is not bothersome. He endorses significant sun exposure in his youth and admits to rarely using sunscreen when he is outdoors. On physical examination, the following is seen (Figure 10-6).



Figure 10-6

For which of the following conditions is this skin condition a precursor?

- (A) Melanoma
- (B) Basal cell carcinoma
- (C) Squamous cell carcinoma
- (D) Cutaneous T-cell lymphoma

**The answer is C: Squamous cell carcinoma.** The patient in this question is presenting with an actinic keratosis, a small and rough papule (erythematous, brownish, or skin-colored) whose risk of carcinoma depends on the degree of epithelial dysplasia. Actinic keratoses are precursors for squamous cell carcinoma, a locally invasive skin cancer that rarely metastasizes. Risk increases with excessive sun exposure and arsenic exposure. (A) Although melanoma is not associated with actinic keratoses, melanoma is also associated with sunlight exposure. Dysplastic nevi are precursors to melanoma. (B) Basal cell carcinomas are not formed from actinic keratoses. Similar to squamous

cell carcinoma, basal cell carcinoma is locally invasive and rarely metastasizes.  
 (D) Cutaneous T-cell lymphoma is not associated with actinic keratoses.

- 8** A 41-year-old woman presents with tender and enlarged lumps on her shins. She also endorses weakness, subjective fevers, and arthralgia. On physical examination, the following is seen (*Figure 10-7*).



**Figure 10-7**

Which of the following is NOT associated with this dermatologic condition?

- (A) Sarcoidosis
- (B) Inflammatory bowel disease
- (C) Streptococcal infection
- (D) Diabetes mellitus type 2

**The answer is D: Diabetes mellitus type 2.** The patient in this question is presenting with erythema nodosum, inflammatory lesions of subcutaneous fat that are usually located on the shins. The nodules are usually tender and typically resolve in 1 to 2 months. (A, B, C) Although the cause of erythema nodosum is commonly unknown, it has been associated with sarcoidosis, inflammatory bowel disease, and streptococcal infection (especially in children). It has also been associated with coccidioidomycosis, histoplasmosis, TB, and leprosy. It is not associated with diabetes.

## General Medicine

1

A 61-year-old man with a history of hypertension asks what measures he can take from a nonpharmacologic perspective to manage his hypertension. The patient reports that he drinks 1 to 2 beers per day and smokes a half pack of cigarettes per day.

Which of the following lifestyle modifications has been shown to result in the greatest reduction in blood pressure?

- (A) Dietary Approaches to Stop Hypertension (DASH) diet
- (B) Weight loss
- (C) Decreasing alcohol consumption
- (D) Increasing exercise
- (E) Smoking cessation

**The answer is B: Weight loss.** The seventh report of the Joint National Committee (JNC 7) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends *all* patients with hypertension (blood pressure of 140/90 mmHg or higher) or prehypertension (blood pressure of 120/80 to 139/89 mmHg) execute five lifestyle modifications: *Reducing dietary sodium* to less than 2.4 g/d; *increasing exercise* to at least 30 min/d (4 d/wk); *limiting alcohol consumption* to 2 drinks or less per day for men and 1 drink or less per day for women; following the *Dietary Approaches to Stop Hypertension (DASH) diet* (high in fruits, vegetables, potassium, calcium, and magnesium; low in fat and salt); and achieving a *weight loss* goal of 4.5 kg (10 lb) or more. Of these, weight loss has shown to have the highest reduction in systolic blood pressure (reduction from 5 to 20 mmHg) in overweight patients. (A, C, D) These three lifestyle modifications are also recommended and do have a substantial effect on reduction of systolic pressure, just not as much as weight loss does. (E) Smoking cessation should always be encouraged as part of any comprehensive lifestyle modification plan.

2

A 51-year-old man presents for a routine annual physical examination. The patient only reports constipation, but says it has been present for several years. He has an insignificant past medical history and reports

smoking 2 packs of cigarettes per day for the last 15 years. He also drinks 2 to 3 beers per day. Physical examination is within normal limits. A colonoscopy is performed as part of the routine screening measures and demonstrates several diverticular outpouchings in the sigmoid colon. The patient is educated on diverticulosis.

Which of the following is the best recommendation to give to this patient for his newly diagnosed disease?

- (A) Increase iron intake
- (B) Increase fiber intake
- (C) Smoking cessation
- (D) Decrease alcohol consumption

**The answer is B: Increase fiber intake.** This patient has asymptomatic diverticulosis. A diverticulum is a pouch (or sac) that protrudes from the colonic wall at a point of weakness. Diverticulosis is often asymptomatic, but can present with constipation, abdominal pain, and painless rectal bleeding. The treatment for asymptomatic diverticulosis is lifestyle modification in the form of increased fiber intake. Fiber allows for the creation of large, bulky stools that increase the width of the colon and minimize the likelihood of diverticular development. (A) Increased iron intake is not part of the treatment of diverticulosis. (C, D) Smoking cessation and decreasing alcohol consumption should always be encouraged as part of any comprehensive lifestyle modification plan, but do not have any proven effect on diverticulosis.

**3** Over the last 10 years, more people in the town of Nankville appear to be suffering from Hodgkin lymphoma than in the town of Gridora.

Which of the following types of studies is best for calculating the difference in incidence between Nankville and Gridora?

- (A) Cross-sectional
- (B) Case-control
- (C) Cohort
- (D) Clinical trial

**The answer is C: Cohort.** In this question, we need to find the study that is best for calculating the incidence (the frequency of new cases of a particular disease that arise in a population *at risk* over a certain time period). One can infer that in order to figure out the incidence, people *without* the disease need to be followed over a certain time period to determine how many of them develop that disease of interest. The best choice is a cohort study, a prospective observational study. Once residents in Nankville and Gridora have been followed over a certain time period, the incidence of Hodgkin lymphoma can be determined. Furthermore, the comparison of incidences will allow one to calculate the *relative risk* for developing Hodgkin lymphoma in one town versus the other.

(B) Case-control is retrospective and patients with the disease (cases) are compared to patients without the disease (controls). Information is collected about *previous* exposure to risk factors. Case-control studies allow for calculation of odds ratio, but not incidence. (A) Cross-sectional studies are studies *at one point in time*, so these studies are ideal for measuring a disease's *prevalence* (total number of cases in a population). (D) Clinical trials are used to determine the benefit of an intervention (drug, procedure, etc.) in patients *who already have* the disease. They do not determine incidence.

**4** A 22-year-old woman presents for a routine annual physical examination. She has no complaints. She smokes 2 packs of cigarettes per day and drinks 2 glasses of wine per day. She is sexually active with one male partner and two female partners. She reports using oral contraceptive pills for birth control and consistent condom use with her male partner. Her family history is significant for breast cancer on her maternal side (aunt) and colon cancer on her paternal side (father died of colon cancer at the age of 52).

What is the recommended screening measure at this patient's visit?

- (A) Colonoscopy
- (B) *Chlamydia trachomatis* screening
- (C) Lipid panel
- (D) Mammogram

**The answer is B: *Chlamydia trachomatis* screening.** This patient is presenting for a routine physical examination and it must be determined what screening measures are recommended at this time. The U.S. Preventive Services Task Force (USPSTF) in 2007 recommended routine screening for *Chlamydia trachomatis* infection in all sexually active women who are 24 years and younger, in addition to asymptomatic women of all ages who are at increased risk for sexually transmitted infections (including those with sexually transmitted infections and those with new and/or several sexual partners). (A) Although this patient has a family history of colon cancer, the USPSTF recommends colon cancer screening starting at 50 years of age. However, if there is family history in a *first-degree* relative, then it should be initiated 10 years before the age of that relative's diagnosis or 40 years of age, whichever comes first. This patient should have her first colonoscopy at the age of 40 (her father got it at 52 years of age, and 52 minus 10 is 42, so 40 comes before 42). (C) Lipid panel screening is recommended by the USPSTF for men of age 35 and older and women of age 45 and older (those with risk factors can be screened earlier at the age of 20). (D) Mammogram screening per USPSTF recommendations should begin at the age of 50 and older and occur every 2 years (for those with average risk). Of note, recommended immunizations for this patient include the Tdap booster and HPV vaccination (if not already done).



- 5 A prospective cohort study was performed to determine the relative risk of radiation exposure on squamous cell carcinoma (SCC) of the skin in elderly Caucasian men. The results showed that radiation exposure increased the risk of cutaneous SCC with a relative risk of 0.76 and  $p$ -value of 0.035.

Which of the following is a serious limitation of this study?

- (A) Internal validity
- (B) External validity
- (C) Reliability
- (D) Measurement bias

**The answer is B: External validity.** External validity, also known as generalizability, is the applicability of the results of the study to other populations. In other words, it extends the results beyond the cohort being studied. In this study, the external validity is clearly limited (restricted to elderly Caucasian men). (A) Internal validity is the validity of the study within the cohort itself. (C) Reliability is synonymous with reproducibility and precision and is defined as the degree to which repeated measurements under unchanged conditions show the same results. (D) Measurement bias is not the best answer because there is no information in this question related to the how the study was actually designed and conducted.

- 6 A cohort study was performed to determine the relationship between elevated LDL levels and the development of a myocardial infarction. After a 7-year follow up trial period, the following data was analyzed (Table 11-1).

**Table 11-1**

|                 | Myocardial Infarction | No Myocardial Infarction | Total |
|-----------------|-----------------------|--------------------------|-------|
| Elevated LDL    | 60                    | 40                       | 100   |
| Nonelevated LDL | 20                    | 80                       | 100   |
| Total           | 80                    | 120                      | 200   |

Which of the following is the 7-year risk of getting a myocardial infarction in patients with elevated LDL levels?

- (A) 0.2 (20%)
- (B) 0.3 (30%)
- (C) 0.4 (40%)
- (D) 0.6 (60%)



**The answer is D: 0.6 (60%).** Risk is essentially a measure of the *incidence* of the disease. Note that in this question we are looking for *risk* as opposed to *relative risk*. Risk is calculated by dividing the number of patients with the disease (myocardial infarction) by the overall number of patients at risk (so 60 divided by 100). (A) 0.2 (20%) is the risk of getting a myocardial infarction in patients *without* elevated LDL levels. (B) 0.3 (30%) is the *relative risk* of getting a myocardial infarction in those patients with elevated LDL levels (here we divide the risks in each groups by each other, so 0.6 divided by 0.2). (C) 0.4 (40%) is the 7-year risk of getting a myocardial infarction in *all* patients in this study (80 divided by 200). Absolute risk reduction (ARR) is essentially the *risk difference* and here would be the difference between the two groups' risks ( $0.6 - 0.2 = 0.4$ ). ARR is the inverse of number needed to treat (NNT), so to find NNT, we divide 1 by 0.4 and *round up*. 1 divided by 0.4 is 2.5, so NNT is 3.

7

A 62-year-old man presents with a 3-month history of weakness, fatigue, and weight loss. He also reports a burning epigastric pain. The patient has an insignificant past medical history and smokes 2 packs of cigarettes per day. He drinks 4 to 5 beers per day as well. Work-up is initiated and the patient is found to have a positive fecal occult blood test. Esophagogastroduodenoscopy is performed and demonstrates a fundal ulcer. Biopsy is performed and is positive for adenocarcinoma.

Which of the following is the best next step in management of this patient?

- (A) *H. pylori* serologic testing
- (B) CT scan
- (C) Laparoscopy
- (D) Hospice referral

**The answer is B: CT scan.** When a malignancy is diagnosed histologically, it is critical to determine the extent of the malignancy to aid in timely and correct patient care. In patients with newly diagnosed gastric cancer, CT scan is the modality of choice to evaluate for the extent of the disease. The stage will allow the physician to determine the most appropriate therapy. CT is employed due to its high sensitivity in determining metastases (particularly liver metastases). (A) *H. pylori* is strongly associated with gastric lymphoma, not in adenocarcinoma. (C) Laparoscopy could be used *after* CT scan is performed to detect metastases not noticed on the CT scan. (D) It is too early to determine the need for hospice care and prognosis without accurately staging the disease.

8

A 22-year-old man presents with headache, vomiting, and confusion. His girlfriend reports that he was at a local bar that was hosting a barbeque. Due to inclement weather, the barbecue was held indoors. Physical

examination reveals a heart rate of 112 beats per minute, respiratory rate of 24 breaths per minute, and diffusely pink skin.

Which of the following is the most likely diagnosis in this patient?

- (A) Cyanide poisoning
- (B) Carbon monoxide poisoning
- (C) Methemoglobinemia
- (D) Arsenic poisoning

**The answer is B: Carbon monoxide poisoning.** This patient is presenting a history highly consistent with carbon monoxide poisoning (smoke inhalation from several sources such as automobiles, furnaces, and even charcoal grills). Carbon monoxide prevents organs and tissues from using oxygen effectively. Acute symptoms include headaches, vomiting, abdominal pain, confusion, and sometimes coma. Dermatologic findings include a pinkish-red skin hue. Diagnosis is confirmed by ordering carboxyhemoglobin levels and treatment is with supplemental oxygen. Another very important clue to the diagnosis of carbon monoxide poisoning includes several people presenting at the same time with similar symptoms who were in the same confined quarters.

(A) Cyanide poisoning occurs from burning of rubber or plastic and is associated with a stereotypical “bitter almond breath.” Given that the symptoms are highly similar to carbon monoxide poisoning, clinical history is crucial! (C) Methemoglobinemia can occur from drugs and environmental exposures, and unlike carbon monoxide and cyanide, it is characterized by a cyanosis and bluish discoloration of the skin.



A 29-year-old woman is brought to the Emergency Department after falling from the balcony located on the third story of her apartment building. She reports severe abdominal pain and distention is noted on physical examination. Urgent laparotomy confirms a splenic laceration and a splenectomy is performed. The patient does well postoperatively.

Which of the following vaccines is recommended in this patient?

- (A) Hepatitis A
- (B) Pertussis
- (C) *Salmonella typhi*
- (D) Meningococcal

**The answer is D: Meningococcal.** This patient has undergone a splenectomy and is now at significant risk for infection caused by the encapsulated organisms. The mnemonic “SHiNKS” can help one recall several of these organisms: *S. pneumoniae*, *H. influenzae*, *N. meningitidis*, *Klebsiella*, and *Salmonella*. Without the spleen, phagocytes are unable to recognize and “engulf”

these organisms, so patients who have received a splenectomy must receive several vaccinations. The ones that are commonly given are vaccinations against *S. pneumoniae*, *H. influenzae*, and *N. meningitidis*. (A, B) These vaccines should be given in different contexts (Hepatitis A for travel to endemic areas and patients with chronic liver disease; Pertussis is in the standard childhood vaccination series). Neither of these organisms pose risk specifically for an asplenic patient. (C) Although *Salmonella typhi* is encapsulated, vaccination is only necessary for travelers to endemic countries (no current recommendation for postsplenectomy patients).

10

Several academic dermatologists are conducting a study to determine the risk factors for acral lentiginous melanoma versus superficial spreading melanoma. A hundred and twenty patients are identified with a diagnosis of acral lentiginous melanoma and 140 patients are identified with a diagnosis of superficial spreading melanoma. The researchers subsequently engage in a thorough review of the patients' medical records, demographic characteristics, and family history. They then execute a side-by-side comparison of the differences ascertained between the two groups.

Which of the following is the study design being implemented in this example?

- (A) Retrospective cohort study
- (B) Case-control study
- (C) Prospective cohort study
- (D) Cross-sectional study

**The answer is B: Case-control study.** In this study design, the researchers first determined the *outcome* (acral lentiginous or superficial spreading melanoma). Following identification of the *outcome*, it is only then that they looked for associated risk factors. This is the definition of a case-control study. (A) Retrospective cohort study is very similar to case-control, but the order in which *outcomes* and *risk factors* are determined is opposite. In a retrospective cohort study, risk factor exposure is determined first and then the outcome of interest is determined later. (C) Prospective cohort study is looking *ahead*, not looking back. Subjects with exposure and those without exposure are followed over time to determine the outcome of interest. (D) Cross-sectional studies assess both *exposure (risk factors)* and *outcome* at a single point in time. It is used to determine prevalence. Table 11-2 summarizes the different study types.

Table 11-2

| Study Type      | Study Description                                                                                                                                                                                                                                                                                                                   | Relevant Calculations |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Case-control    | <ul style="list-style-type: none"> <li>First identify outcome (have disease or not), then risk factors</li> <li>Retrospective</li> </ul>                                                                                                                                                                                            | Odds ratio            |
| Cohort study    | <ul style="list-style-type: none"> <li><b>Retrospective Cohort</b> → First identify risk factor, then outcome (have disease or not) <b>[opposite of case-control]</b></li> <li><b>Prospective Cohort</b> → Subjects both with risk factor and those without risk factor are followed over time and compared; looks ahead</li> </ul> | Relative risk         |
| Cross-sectional | <ul style="list-style-type: none"> <li>Both risk factors and outcomes determined at same point in time</li> <li>Neither retrospective nor prospective</li> </ul>                                                                                                                                                                    | Prevalence            |

11

A new testing modality is being considered for measuring blood glucose levels. If a patient's true blood glucose level is 86 mg/dL and the new test returns three consecutive results (101 mg/dL, 99 mg/dL, and 100 mg/dL), what can you conclude about this new test?

- (A) Neither reliable nor accurate
- (B) Reliable but not accurate
- (C) Accurate but not reliable
- (D) Reliable and accurate

**The answer is B: Reliable but not accurate.** Distinguishing reliability from accuracy is very important for study analysis. A reliable test essentially gives *very close* (almost the same) results on repeat measurement. Reliability is also synonymous with reproducibility and precision. The test generated three very similar blood glucose levels, therefore the test is reliable. However, the patient's *true* level is 86 mg/dL. An accurate test is one that measures the *true value* of a test. This test is not close to the true level of 86 mg/dL; therefore the test is not accurate.

12

A study of total cholesterol levels in patients with familial hyperlipidemia shows that the data is normally distributed with a mean of 215 mg/dL and a standard deviation (SD) of 15 mg/dL.

Based on these results, 95% of total cholesterol levels in these patients fall in which of the following ranges?

- (A) 205 and 225 mg/dL
- (B) 210 and 220 mg/dL
- (C) 200 and 230 mg/dL
- (D) 185 and 245 mg/dL

**The answer is D: 185 and 245 mg/dL.** Normally distributed results are symmetric and bell-shaped. Normal distributions are helpful for predicting the percentage of observations that fall within certain limits from the average or mean. This level of deviation from the mean is called standard deviation. 95% of all observations fall within two standard deviations from the mean. In this case, the standard deviation is 15, so  $2 \times 15 = 30$ , and  $215 \pm 30 = 185$  and 245. Using the 68-95-99.7 rule (one SD in each direction from the mean creates a 68% confidence interval, two SDs create a 95% confidence interval, and three SDs create a 99.7% confidence interval), there is a 95% chance that this population will have a reading within the range of 185 to 245 mg/dL (Figure 11-1). (C) 200 and 230 mg/dL would be the answer if the questions were asking for 68% of observations (or *one* standard deviation from the mean).

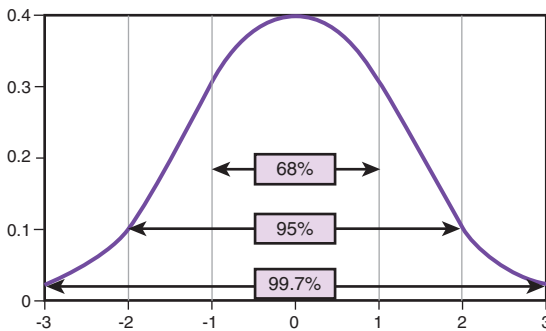


Figure 11-1

13

A study was designed to evaluate a new serologic marker for diagnosing ovarian cancer. Hundred patients with strong family histories of ovarian cancer were selected randomly from the population, screened using the new test, and screened again (using biopsy) to determine the true diagnosis. The findings are summarized below (Table 11-3).

Table 11-3

| Test Results | True Ovarian Cancer | No Ovarian Cancer | Total |
|--------------|---------------------|-------------------|-------|
| Positive     | 5                   | 45                | 50    |
| Negative     | 10                  | 40                | 50    |
| Total        | 15                  | 85                | 100   |

Which of the following is the sensitivity of the new screening test for ovarian cancer?

- (A) 5/15
- (B) 40/85
- (C) 5/50
- (D) 40/50

**The answer is A: 5/15.** Sensitivity tells you of *all patients with TRUE disease state*, how many test positive. It is the measure of true positives divided by (true positives + false negatives). In this case it is 5 divided by 15, or 33%. Sensitivity is used to rule diseases *out* and high sensitivity indicates superior screening value. (B) 40/85 is this test's *specificity*. Specificity tells you of *all patients who do NOT have disease state*, how many truly test negative. It is useful for ruling disease *in*. (C) 5/50 is this test's positive predictive value, which tells you of *all patients who test positive*, how many truly have the disease state; it is measured by taking the true positives and dividing by (true positives + false positives). (D) 40/50 is this test's negative predictive value, which tells you of *all patients who test negative*, how many do not have the disease state. It is important to remember that the positive and negative predictive values depend on the prevalence of the disease in the population, whereas sensitivity and specificity are characteristics of the diagnostic test itself and are thus unchanged by the prevalence of the disease.

**14** A study was conducted to evaluate a new test intended for confirmation of tuberculosis infection after a positive purified protein derivative (PPD). The study data revealed a sensitivity of 95%, a specificity of 25%, a positive predictive value of 90%, and a negative predictive value of 85%.

Which of the following can be said about this new test?

- (A) Accurate test for screening but not for confirmation of disease
- (B) Inaccurate test for both screening and confirmation
- (C) Inaccurate test for screening but accurate for confirmation of disease
- (D) Accurate test for both screening and confirmation

**The answer is A: Accurate test for screening but not for confirmation of disease.** This test generates a high sensitivity (95%) and a low specificity (25%). Sensitivity is a valuable metric for *screening* diseases, and specificity is a valuable metric for the *confirmation* of diseases (*sensitivity rules out* and *specificity rules in*—“*sn-out*” and “*sp-in*”). Therefore, the new test in this question would be excellent for screening tuberculosis infection but not for final confirmation of the disease. **(B)** This would be the answer if both sensitivity and specificity were low. **(C)** This would be the answer if this test had a high specificity and a low sensitivity. **(D)** This would be the answer if both sensitivity and specificity were high.

15

A 49-year-old man presents for routine physical examination. The patient has no active complaints today other than occasional constipation and increased frequency of urination. The patient reports that he has a diagnosis of “pre-diabetes” given to him by his previous physician in another city. His family history is significant for hypertension. The patient denies alcohol or drug use and works as a long-distance truck driver. Physical examination is unremarkable except for a body mass index of 31 kg/m<sup>2</sup>. The patient’s fasting laboratory values reveal the following.

|                               |           |
|-------------------------------|-----------|
| Hemoglobin A1c                | 7.9%      |
| Serum glucose                 | 170 mg/dL |
| Total cholesterol             | 220 mg/dL |
| Low-density lipoprotein (LDL) | 145 mg/dL |
| Triglycerides                 | 130 mg/dL |
| High-density lipoprotein      | 38 mg/dL  |

Which of the following is the best next step in the management of this patient?

- (A)** Lifestyle modification
- (B)** Atorvastatin and lifestyle modification
- (C)** Sulfonylurea
- (D)** Niacin, fish oil, and lifestyle modification

**The answer is B: Atorvastatin and lifestyle modification.** This patient is presenting with a new diagnosis of type 2 diabetes mellitus (T2DM) given his symptoms (frequency of urination), increased fasting glucose, and elevated hemoglobin A1c. Patients with diabetes are at significant risk for cardiovascular atherosclerotic events. Therefore, patients who are greater than the

age of 40 with diabetes should be on a statin medication (atorvastatin) and begin intensive lifestyle modification (exercise, diet). (C) A sulfonylurea (e.g., glimepiride) is not the initial drug of choice with new-onset diabetes. Metformin therapy is recommended after diagnosing T2DM. (D) Niacin is helpful in raising high-density lipoprotein, but can actually worsen glucose control in diabetics. Fish oil is helpful in reducing serum triglycerides but does not have an effect on improving cardiovascular outcomes.

16

A 39-year-old man presents for his annual physical examination. He has a history of asthma, pre-hypertension, and Gilbert syndrome. The patient smokes a pack of cigarettes per day, but is pleased because he has cut it down from 2.5 packs per day. He has smoked since the age of 20. The patient is motivated at this visit to seek assistance in smoking cessation.

Which of the following medications can help him quit smoking in both the short and long term?

- (A) Propranolol
- (B) Buspirone
- (C) Bupropion
- (D) Paroxetine

**The answer is C: Bupropion.** Bupropion is a drug primarily used as an atypical antidepressant and is used in smoking cessation. It is the most commonly used medication in increasing short- and long-term smoking cessation rates. Of note, varenicline is another smoking cessation medication that is thought to be even more effective than bupropion in short- and long-term smoking cessation rates. Varenicline acts via partial agonism of nicotinic acetylcholine receptors. Nicotine-replacement therapy, either alone or in addition to bupropion or varenicline, can also be used and may be more effective than using either medication alone. Bupropion is unique compared to the other antidepressant drugs in that it has no sexual side effects. It should not be used in bulimic patients and those at risk of seizures because it can lower the seizure threshold. (A) Propranolol is a nonselective  $\beta$ -blocker used in several clinical contexts, but not in smoking cessation. (B) Buspirone is an anxiolytic psychoactive drug and is primarily used to treat generalized anxiety disorder. Some researchers postulate some efficacy of buspirone in smoking cessation but data is still limited. (D) Paroxetine is an SSRI used in depression; SSRIs have not been shown to work for smoking cessation.

17

A 9-year-old boy presents with his mother for a health evaluation. They just moved from China and the mother reports that her family has experienced many deaths from cancer and she is concerned about her



child's health. Physical examination reveals a healthy boy with unremarkable findings. Laboratory values are all within normal limits.

Which of the following vaccines can be given to this patient to reduce his risk of developing cancer?

- (A) Measles, mumps, and rubella (MMR) vaccine
- (B) Hepatitis B vaccine
- (C) Hepatitis A vaccine
- (D) Polio vaccine

**The answer is B: Hepatitis B vaccine.** Of the four choices, only hepatitis B vaccine can diminish the risk of developing cancer. Chronic hepatitis B infection can cause hepatocellular carcinoma (HCC). In parts of Asia, chronic hepatitis B infection is most often caused by vertical transmission from mother to child. In the United States, however, it is most often contracted through blood (needlesticks, sexual intercourse, etc.). Vaccination against hepatitis B ensures that the virus is never contracted and therefore prevents the development of HCC. Importantly, there are two infections that increase the rate of cancer for which there are vaccines: Hepatitis B and HPV. (A, C, D) The other choices do not protect against any cancers.



A 69-year-old woman presents for a routine physical examination. The patient feels well and has no active complaints today. She has never smoked and does not drink alcohol. The patient has an insignificant past medical history and says she feels “blessed” because everyone in her family has “died of old age.” Two years ago at her last appointment, the patient had a mammogram (normal result), Pap smear (normal result), and lipid panel. She had a colonoscopy 8 years previously that showed no lesions or polyps.

Which of the following should be performed at this visit?

- (A) Colonoscopy
- (B) Lipid panel
- (C) Mammogram
- (D) Pap smear

**The answer is C: Mammogram.** According to the USPSTF, mammograms should be performed every 2 years for women between the ages of 50 and 74. Furthermore, beyond the age of 75, routine mammograms are not recommended and should only be performed in case-by-case situations. This patient received her last mammogram 2 years ago and therefore is due for another. (A) Colonoscopy should be performed every 10 years between the ages of 50 and 75. This patient had a normal colonoscopy 8 years ago. (B) Lipid panel screening should be performed in men starting at 35 years (average risk) and in women starting at 45 years (average risk). Performing

lipid screening every 5 years is currently recommended. This patient had a lipid panel 2 years ago. **(D)** Pap smears can be discontinued at the age of 65 if the patient received adequate screening up to that age without evidence of premalignancy/malignancy.

**19** A 29-year-old medical student is injured via needlestick while drawing blood from a patient with chronic hepatitis B. The patient received his final hepatitis B vaccination of the series 8 years ago. The patient had his titers checked before clinical rotations 6 months ago and was found to be positive for anti-hepatitis B surface antibodies (HBsAb).

Which of the following is the best next step in the management of this patient?

- (A)** Hepatitis B immunoglobulin (HBIG) now
- (B)** Serologic testing for HBsAg
- (C)** Hepatitis B vaccination
- (D)** Reassurance

**The answer is D: Reassurance.** This patient demonstrates immunity to hepatitis B (positive for HBsAb) and therefore reassurance should be offered. Immunity to hepatitis B occurs when anti-hepatitis B surface antibodies (HBsAb) develop against the recombinant hepatitis B surface antigen. Given the patient's documented hepatitis B vaccination and positive titers for HBsAb, reassurance is appropriate. **(A, C)** If the patient had unknown vaccination history, he should receive *both* HBIG (passive immunity) and hepatitis B vaccine (active immunity). **(B)** The patient has documentation already revealing positivity for HBsAb. Therefore, a hepatitis B panel is unnecessary. The patient should be tested for HIV and HCV as well, and HIV postexposure prophylaxis should be considered.

**20** A 60-year-old man presents for his annual physical examination. The patient feels well and has no active complaints. The patient takes atorvastatin for hyperlipidemia. The patient has no family history of cancer. His blood pressure is 128/64 mmHg and his pulse is 82/min. A digital rectal examination is performed and shows an enlarged, smooth prostate. Fecal occult blood test is negative. The patient had a colonoscopy 7 years ago that was normal. His lipid panel was within normal limits at his last visit 1 year ago.

Which of the following is the best next step in managing this patient?

- (A)** PSA testing
- (B)** Biopsy of prostate and PSA testing
- (C)** Ultrasound of prostate
- (D)** Conversation with the patient regarding PSA testing

**The answer is D: Conversation with the patient regarding PSA testing.** The current guidelines for prostate cancer screening are slightly controversial. The USPSTF currently does not recommend screening with PSA for any age. The USPSTF justifies this recommendation by citing the high rate of false positives, causing further unnecessary tests and procedures that lead to significant pain and side effects (impotence and incontinence). Although several associations differ with respect to prostate screening guidelines, screening decisions should be discussed with the patient so he can decide based on the known risks and benefits of screening with PSA.

21

A 64-year-old woman presents to the physician with the request of being screened for bladder cancer. She feels well and has no complaints, but her sister just passed away from bladder cancer and she would like to determine if she has it as well. She smokes 2 packs of cigarettes per day and drinks 2 to 3 glasses of red wine per day. Physical examination shows an obese woman with wheezing on lung auscultation and an increased expiratory phase.

Which of the following is the most appropriate next step in management based on this patient's request?

- (A) Bladder tumor antigen testing
- (B) Urinalysis (UA)
- (C) Urinalysis (UA) and cytology
- (D) No screening

**The answer is D: No screening.** Although bladder cancer is the second most common urologic cancer, the USPSTF does not recommend screening for bladder cancer. The recommendations are based on the fact that the current screening modalities (UA, cytology, bladder tumor antigen) all have low incidence and very low positive predictive value. Therefore, screening for bladder cancer is not recommended even in those patients at risk for developing the disease (cigarette smoking, industrial chemical exposure, etc.).

22

A 67-year-old man presents to the physician for his annual health maintenance examination. The patient feels well and has no active complaints. He has a history of type 2 diabetes and hypertension. He smoked a pack of cigarettes per day for 5 years (between the ages of 34 and 39). He drinks 1 to 2 beers per day but denies any illicit drug use. He is up-to-date on his colonoscopy screening and lipid panel screening. He has been reading about abdominal aortic aneurysms and would like to know if he should be screened or not for this disease.

Which of the following is the next step with respect to this patient's inquiry?

- (A) Reassurance
- (B) CT scan of abdomen
- (C) Ultrasound of the abdomen
- (D) MRI of abdomen

**The answer is C: Ultrasound of the abdomen.** The USPSTF recommends a single screening ultrasound for abdominal aortic aneurysm (AAA) in men aged 65 to 75 years who have any history of smoking. AAAs are often asymptomatic until they rupture, which has a high mortality rate when this occurs; therefore, screening in this group is highly recommended. Ultrasound is the best modality since it is noninvasive and cost-effective. A surgical intervention is often recommended if the aneurysm grows more than 1 cm per year or if it is bigger than 5.5 cm. Of note, screening is not recommended in women.

**23** A 27-year-old man presents to the physician for a travel medicine appointment. The patient will be visiting several developing countries in North Africa for 2 months as part of an anthropologic research endeavor. The patient has an insignificant past medical history and drinks 2 to 3 beers per week. He has never traveled outside of the United States before. Physical examination is unremarkable.

Which of the following should be offered to this patient at this time?

- (A) Meningococcal vaccine
- (B) Pneumococcal vaccine
- (C) Hepatitis A vaccine
- (D) Yellow fever vaccine

**The answer is C: Hepatitis A vaccine.** Travel medicine appointments are critical in order to determine what infectious diseases travelers will be exposed to in their destination. The risk of contracting hepatitis A is pronounced for those travelers going to *developing countries* and this patient should receive vaccination against hepatitis A. A one-time dose of hepatitis A vaccine offers short-term protection for a young adult; however, a second dose should be administered for long-term immunity. (A) Meningococcal vaccine might be necessary for travelers going to Asia and sub-Saharan Africa, but not North Africa. (B) Pneumococcal vaccine is recommended for young children, those older than 65 years of age, and young adults with certain chronic diseases. (D) Yellow fever vaccine is to protect against a mosquito-borne viral hemorrhagic fever. This is endemic to tropical regions of sub-Saharan Africa and parts of South America.

24

A 37-year-old HIV positive man presents for a routine visit. He is new to this city as his job relocated him and he is here to establish care. He contracted HIV through intravenous drug use 15 years ago. He is married to his wife of 10 years who is HIV negative. They have a monogamous sexual relationship. The patient is diligent with his HIV medications and endorses “100% safety” with sexual intercourse with his wife to ensure no transmission. The patient reports that he received all his childhood vaccinations and immunizations. He feels well today and has no active complaints.

Which of the following vaccinations is appropriate to offer to this patient today?

- (A) Meningococcal vaccine
- (B) Hepatitis A vaccine
- (C) Tetanus and diphtheria toxoid booster
- (D) No vaccination today

**The answer is C: Tetanus and diphtheria toxoid booster.** It is critically important to understand vaccinations in the HIV positive population. Several vaccines are beneficial to HIV positive patients and several are contraindicated. All HIV positive patients should receive the influenza virus vaccine and the hepatitis B vaccine at diagnosis. Pneumococcal vaccine should also be administered. Furthermore, the meningococcal vaccine, HPV vaccine, and *H. influenzae* type B vaccine are administered in the *same* guidelines as all adults. Similarly, patients with HIV should receive a tetanus and diphtheria toxoid booster every 10 years. Since the patient last received vaccines in childhood (>10 years ago), he should receive a tetanus and diphtheria toxoid booster.

(A) Meningococcal vaccine in HIV positive patients is administered according to the same guidelines as all adults (college age, living in dormitories or barracks, asplenic individuals, and certain travel destinations). (B) Hepatitis A vaccine is administered to *men who have sex with men*. This patient is monogamous with his wife and contracted HIV through intravenous drug use. It actually would be a good idea to give this patient hepatitis A vaccination, but this is not the best answer. (D) No vaccination is inappropriate. The patient should get influenza virus vaccine, the hepatitis B vaccine, pneumococcal vaccine, and tetanus and diphtheria toxoid booster.

25

A 65-year-old woman presents to the physician for her annual physical examination. The patient is up-to-date on vaccinations and had a mammogram done at her previous appointment 1 year ago that was normal. She had a colonoscopy performed 6 years ago that was normal. The patient is otherwise healthy and reports drinking 1 to 2 glasses of wine per week with her girlfriends at their weekly lunch outing.

Which of the following should be recommended to this patient at her visit today?

- (A) Mammogram
- (B) Colonoscopy
- (C) Calcium and phosphorus levels
- (D) Dual-energy x-ray absorptiometry (DEXA)

**The answer is D: Dual-energy x-ray absorptiometry (DEXA).** Risk factors for osteoporosis include smoking, family history, low body weight, excessive alcohol use, and secondary organic causes such as premature menopause, among others. Although this patient is not demonstrating risk factors for developing osteoporosis, the USPSTF recommends a one-time screening for osteoporosis in *all* women aged 65 years or older with DEXA scan of the spine and hips. A bone density with T-score  $<2.5$  standard deviations below the mean is associated with osteoporosis and a T-score between 1 and 2.5 standard deviations below the mean is associated with osteopenia. (A) The patient had a normal mammogram the year before. Mammograms should be performed every 2 years in her age group. (B) The patient had a colonoscopy 6 years ago that was normal. She is due for another colonoscopy in 4 years (reaching the 10-year mark after her previous one). (C) Calcium and phosphorus levels are normal in patients with osteoporosis and have no value in screening for the condition.

26

A 65-year-old man presents for a routine health maintenance examination. The patient endorses moderate wheezing and shortness of breath. He has smoked 3 packs of cigarettes per day for the past 40 years and is being treated for COPD. He drinks 3 to 4 beers per day. The patient has a family history of pancreatic cancer (his brother passed away from pancreatic cancer 2 years ago). He would like to be screened today for pancreatic cancer.

Which of the following is the screening test of choice for pancreatic cancer?

- (A) No screening recommendations
- (B) Abdominal ultrasound one time between 65 and 75 years of age
- (C) Abdominal CT scan one time between 65 and 75 years of age
- (D) Annual CA 19 to 9 levels starting at age 45

**The answer is A: No screening recommendations.** Although pancreatic cancer has a high mortality rate (up to 98% 5-year mortality), no blood test or imaging modality have been shown to be effective in screening for pancreatic cancer in asymptomatic patients. It usually presents at an advanced or metastatic stage and presents with several vague nonspecific symptoms. Interestingly, close to 8% of patients with pancreatic cancer have

a family history, so much research is being devoted to finding a screening test. (B) This is the screening test for abdominal aortic aneurysm (AAA). (D) CA 19 to 9 is a protein specific to the pancreatic cancer cells, but is not useful as a screening marker. Rather it is best implemented as a marker of response to treatment.

27

A 29-year-old woman presents for a routine health maintenance examination. She feels well and other than some mild dyspnea with exertion has no active complaints. She reports that she is concerned about getting colon cancer since her father died at the age of 47 from advanced colon cancer (after being diagnosed at the age of 46). She wants to know when she should be screened for colon cancer.

Which of the following is the most appropriate screening for this woman?

- (A) Colonoscopy now
- (B) Colonoscopy at age 36
- (C) Colonoscopy at age 40
- (D) Colonoscopy at age 50

**The answer is B: Colonoscopy at age 36.** According to both the USPSTF and the American Cancer Society, the recommend screening for colorectal cancer is between the ages of 50 and 75 years with sigmoidoscopy every 5 years, colonoscopy every 10 years, or annual fecal occult blood testing. The most sensitive and specific test is colonoscopy. For those at high risk, particularly those with an affected first-degree relative, *screenings begin at the age of 40 or 10 years before the age the relative was diagnosed*. In this case, the patient's father was diagnosed at the age of 46, so she should get her first colonoscopy at the age of 36 (46 minus 10). (C) Colonoscopy at the age of 40 is recommended in high-risk patients (unless the age of the affected relative is lower than 50 at which point screenings should begin earlier (subtract 10 from the age)). (D) Colonoscopy at age 50 is the right answer for screening of a patient with average risk of developing colon cancer.

28

A 59-year-old woman suffers from traumatic brain injury and is admitted to the intensive care unit. She is unresponsive to commands and a gastrostomy tube is placed for feedings.

Which of the following is the best way to prevent decubitus ulcers in this patient?

- (A) Prophylactic antibiotics
- (B) Reposition patient every 2 hours
- (C) Pneumatic compression devices
- (D) Use standard mattresses rather than air and foam

**The answer is B: Reposition patient every 2 hours.** Decubitus ulcers, also known as pressure ulcers, are localized injuries to the skin that usually occur over a bony prominence as a result of pressure. Patients at risk are those that are critically ill and suffering from immobility, poor nutrition, and sensory impairment secondary to diabetes or other two states. The best way to prevent decubitus ulcer formation is to reposition the patient every 2 hours (the point at which tissue damage occurs is 2 hours after entering a new position). (A) Antibiotics would be helpful in treating *infected* ulcers, but not recommended to prevent decubitus ulcers. (C) Pneumatic compression devices are used to prevent deep venous thromboses in patients with venous insufficiency. (D) On the contrary, air and foam mattresses *should* be used to prevent decubitus ulcers since they sufficiently distribute pressure over a larger area.

29

A 41-year-old woman with HIV presents for routine examination. She feels well and has no active complaints. Her recent CD4 count is  $550/\text{mm}^3$  and her viral load is 3,000 copies/mL. Routine titers are drawn and show that the patient has no immunity against mumps or measles.

Which of the following is the next best step in the management of this patient?

- (A) Administer the measles, mumps, rubella (MMR) vaccine today
- (B) Administer the MMR vaccine once CD4 count reaches  $600/\text{mm}^3$
- (C) Do not the administer MMR vaccine
- (D) Explain that MMR vaccine can only be administered in children

**The answer is A: Administer the measles, mumps, rubella (MMR) vaccine today.** Given that patients with HIV are at significant risk for several infections, they should receive several vaccinations at the time of diagnosis (influenza, hepatitis B, pneumococcal). Nonetheless, several live vaccines are *contraindicated* in patients with HIV. The MMR vaccine is one of the live vaccines; however, it can be administered to HIV positive patients with a CD4 count of  $200/\text{mm}^3$  or greater (and without evidence of AIDS-distinguishing illness). The reason that the live MMR vaccines is administered to HIV positive patients is that measles can be life-threatening to HIV positive patients. Live vaccines that are always *contraindicated* in HIV positive patients are BCG, anthrax, oral typhoid, oral polio, intranasal influenza, and yellow fever vaccines.

30

A 3-year-old boy presents to the physician and is diagnosed with *Bordetella pertussis*. His mother endorses that he has had several unpredictable coughing episodes. He is given azithromycin for treatment. He lives in the same house with his parents and two sisters (ages 5 and 7). All family members are current on their immunizations.



Which of the following is the recommended treatment for his family members?

- (A) Administer azithromycin to the sisters
- (B) Administer azithromycin to all family members
- (C) Initiate contact precautions until symptoms resolve
- (D) No prophylaxis needed for family members

**The answer is B: Administer azithromycin to all family members.**

*Bordetella pertussis* is very contagious and is transmitted via respiratory secretions and droplets. Treatment is with a macrolide antibiotic (azithromycin, clarithromycin, or erythromycin) and should be initiated as soon as possible to shorten the course. Even though immunization can prevent the vast majority of pertussis cases, exposed family members can still develop symptoms since immunity wanes over time. (A, C, D) As a result, prophylactic antibiotics (macrolides) are recommended for all close contacts regardless of vaccination status. Furthermore, close contacts who are not fully immunized should also receive the pertussis vaccination.



## Practice Examination

1

A 49-year-old man presents to the physician with fever, confusion, and abdominal pain. His wife explains that for the past few days he has had fevers, night chills, and fatigue, but suddenly developed confusion this morning. His medical history is significant for hypertension and diabetes, for which he takes losartan, amlodipine, and metformin. He denies any tobacco, ethanol, or drug use. His vitals show a temperature of 38.4°C, a blood pressure of 142/90 mmHg, a heart rate of 96 beats per minute, and a respiratory rate of 16 breaths per minute. He has poor dentition, no jugular venous distention, and a normal pulmonary examination. There is a 3/6 holosystolic murmur heard over the apex. Blood cultures are drawn, and the patient is started on empiric antibiotics. A transthoracic echocardiogram shows a normal ejection fraction with no valvular lesions.

What is the most appropriate next step in management of this patient?

- (A) Transesophageal echocardiogram
- (B) Immediate surgery
- (C) CT scan of the chest and abdomen
- (D) Serum erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)
- (E) Intravenous corticosteroids

**The answer is A: Transesophageal echocardiogram.** The patient in this vignette meets one major and two minor of the modified Duke criteria for infective endocarditis (new regurgitant murmur, fever, and poor dentition and diabetes as predisposing conditions). Transesophageal echocardiography (TEE) has a much higher sensitivity to detect infective endocarditis than a transthoracic echocardiogram (TTE), and thus should be performed if the TTE is negative but there is still a high clinical suspicion for the diagnosis. (B) Surgery should be performed if there is serious valvular

dysfunction (e.g., cardiogenic shock), recurrent emboli despite antibiotics, infection with specific organisms that are difficult to treat with antibiotics alone, and a few other indications that are not as high yield. (C) A CT scan of the chest would not be helpful to make a diagnosis at this point. (D) These tests are nonspecific markers of inflammation and would not be very useful in confirming or ruling out infective endocarditis. Elevation in these markers is a minor criterion in the modified Jones criteria for rheumatic fever. (E) IV steroids should not be given in this condition since there is active infection.

2

A 62-year-old man with a history of GERD and peptic ulcer disease presents with severe upper abdominal pain. The patient reports that the pain abruptly started 6 hours ago while he was eating breakfast. He reports diffuse pain that radiates to his back. He has a blood pressure of 100/60 mmHg, pulse of 118/min, temperature of 37.9°C, and a respiratory rate of 24 breaths per minute. On physical examination, there is exquisite tenderness to superficial palpation over the entire abdomen. The patient is unable to tolerate the rest of the abdominal examination.

Which of the following is the best next step in management?

- (A) Ultrasound of the abdomen
- (B) Lipase levels and liver function tests
- (C) CT scan of the abdomen
- (D) Chest x-ray

**The answer is D: Chest x-ray.** With this patient's history of peptic ulcer disease and acute onset abdominal pain, bowel perforation should be suspected. This patient is likely suffering from a perforated peptic ulcer given his inability to tolerate an abdominal examination (guarding and other peritoneal signs may suggest gastrointestinal perforation). The best initial step in management is an upright chest x-ray to detect pneumoperitoneum (chest x-ray will show free air underneath the diaphragm, *Figure 12-1*). Detecting pneumoperitoneum is diagnostic of perforation. (C) If a chest x-ray does not generate positive findings and perforation is highly suspected, proceed with abdominal CT scan. However, chest x-ray should be performed first since it can be done immediately; be cautious of sending patients that may deteriorate to the CT scanner! (A, B) Laboratory tests are too time consuming and would not help diagnose perforation; an ultrasound is not a sensitive test for detecting intestinal perforation.



Figure 12-1

3

A 17-year-old girl presents with 2 weeks of weight loss, intractable nausea and vomiting, and a decreased level of consciousness. She is found to have glucose of 439 mg/dL. She is started on IV fluids and insulin. Four hours later, her laboratory tests demonstrate the following.

|                     |           |
|---------------------|-----------|
| Sodium              | 143 mEq/L |
| Potassium           | 4.2 mEq/L |
| Chloride            | 102 mEq/L |
| Bicarbonate         | 22 mEq/L  |
| Blood urea nitrogen | 14 mg/dL  |
| Creatinine          | 0.9 mg/dL |
| Glucose             | 204 mg/dL |

What is the most appropriate next step in management?

- (A) Switch to subcutaneous insulin glargine
- (B) Continue current management
- (C) Add glucose to the IV fluids
- (D) Switch to oral metformin
- (E) Obtain ECG

**The answer is C: Add glucose to the IV fluids.** This patient has diabetic ketoacidosis (DKA), a frequent presentation of type 1 diabetes mellitus. The main goal in diabetic ketoacidosis is to bring down the blood sugar, hydrate with IV fluids, and closely monitor potassium. Once serum glucose approaches 200 to 250 mg/dL, patients should be given dextrose to help metabolize the serum ketones (note that the patient still has an anion gap). (A) A switch to subcutaneous regular or fast-acting insulin is also reasonable at this time, but long-acting insulin glargine is inappropriate. (D) Oral metformin is used for type 2 diabetes mellitus and is not effective in type 1 diabetes. Although DKA can occur in type 2 diabetes, it is less common. In addition, oral therapy is not appropriate at this time. (E) An ECG would be a good choice in patients with abnormal serum potassium levels.

4

A middle-aged man comes to the Emergency Department complaining of 2 days of shaking chills, as well as a cough with foul-smelling sputum and small amounts of blood. He admits to drinking a pint of vodka and smoking 3 packs of cigarettes each day. He has been to prison twice in the last year. A chest x-ray shows right upper lobe infiltrates. His laboratory tests are shown below.

|                 |                        |
|-----------------|------------------------|
| Hemoglobin      | 13.6 g/dL              |
| Leukocyte count | 16,400/mm <sup>3</sup> |
| Sodium          | 135 mEq/L              |
| Potassium       | 4.2 mEq/L              |
| Creatinine      | 0.9 mg/dL              |
| Glucose         | 110 mg/dL              |

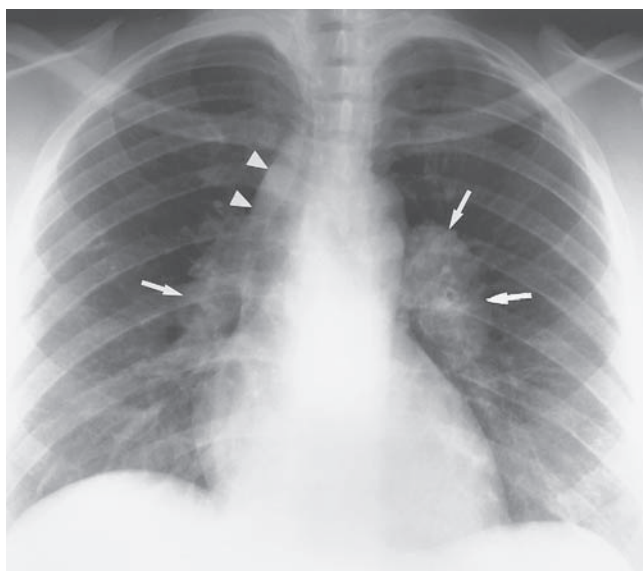
An HIV and tuberculin skin test are both negative. What is the best next step in management?

- (A) Begin ceftriaxone and clindamycin
- (B) Obtain a CT scan of the chest with contrast
- (C) Begin vancomycin and ceftriaxone
- (D) Begin trimethoprim-sulfamethoxazole and prednisone
- (E) Begin rifampin, isoniazid, pyrazinamide, and ethambutol

**The answer is A: Begin ceftriaxone and clindamycin.** This patient's history of alcohol abuse combined with his chest x-ray findings and foul-smelling sputum support a diagnosis of aspiration pneumonia, which should be treated with clindamycin and ceftriaxone to cover both gram-negative and anaerobic pathogens. (B) CT scan of the chest would not change the management. (C) Vancomycin and ceftriaxone is the treatment for health care associated pneumonia; however, the patient has not been hospitalized recently. (D) The patient is HIV negative, making PCP an unlikely diagnosis. (E) Although the patient has risk factors for tuberculosis (TB), the tuberculin skin test was negative.

5

A 33-year-old African American woman complains of fevers, night sweats, and shortness of breath over the past few weeks. Her vital signs are normal, and her lungs are clear to auscultation. She has some waxy skin plaques on her face and erythematous nodules on the anterior portion of her legs. A chest x-ray is performed, which is shown in *Figure 12-2*.



**Figure 12-2**

Which of the following is the likely diagnosis?

- (A) Tuberculosis
- (B) Hodgkin lymphoma
- (C) Pulmonary hypertension
- (D) Sarcoidosis

**The answer is D: Sarcoidosis.** The skin findings and bilateral hilar adenopathy on chest x-ray suggest the diagnosis of sarcoidosis, and African Americans are at an increased risk. Common findings with this disease include hilar lymphadenopathy (biopsy would show noncaseating granulomas) that can produce pulmonary hypertension, erythema nodosum, waxy skin plaques, uveitis, cranial nerve palsies and other neurologic deficits, and many other findings. (A) If the patient had shortness of breath from TB, the chest x-ray would show consolidation (primary TB) or upper lobe infiltrates with or without cavitation (reactivation TB). (B) Thoracic lymphadenopathy could represent lymphoma; however, the association with skin findings makes sarcoidosis more likely. (C) Pulmonary hypertension is a complication of sarcoidosis, and is not the underlying diagnosis. Pulmonary hypertension alone would not produce hilar adenopathy or skin findings.

**6** A 54-year-old man presents with significant eye pain. On further investigation, he recalls multiple episodes of sinusitis. On physical examination, he is noted to have a saddle-nose deformity, a tender, erythematous, and swollen ear, and mild inspiratory stridor. On eye examination, the patient has evidence of scleritis.

What is the most likely diagnosis?

- (A) Sarcoidosis
- (B) Syphilis
- (C) Granulomatosis with polyangiitis
- (D) Polyarteritis nodosa
- (E) Relapsing polychondritis

**The answer is E: Relapsing polychondritis.** (B) Syphilis, granulomatosis with polyangiitis (GPA), and relapsing polychondritis can all present with saddle-nose deformity. The distinguishing feature of relapsing polychondritis is the ear involvement with damage to the auricular cartilage. (C) GPA can present with scleritis, recurrent sinusitis, and pulmonary involvement, but the pulmonary involvement is much more likely to affect lower airways. The patient's inspiratory stridor is more suggestive of upper airway involvement such as tracheobronchomalacia, a life-threatening complication of relapsing polychondritis. (A) Sarcoidosis is less likely to present with the above combination of cartilage inflammation of the ear and scleritis. (D) Polyarteritis nodosa is a vasculitis that presents with generalized symptoms (fatigue, weakness, etc.) and skin rash (ulcerations, palpable purpura, livedo reticularis, etc.).

**7** Shortly after a total thyroidectomy performed for follicular carcinoma, a 61-year-old woman is extubated. Her voice is initially hoarse, and shortly afterward there is a shrill high-pitched noise with each inspiration and she is observed to be gasping for air. There are no signs of swelling at the surgical site. The patient continues to have difficulty breathing and is re-intubated.



What is the most likely etiology of her symptoms?

- (A) Hypocalcemia
- (B) *Haemophilus influenzae*
- (C) Nerve injury
- (D) Hematoma
- (E) Anaphylaxis

**The answer is C: Nerve injury.** Patients undergoing total thyroidectomy are at risk for developing a variety of complications. In this case the patient presents with signs of bilateral recurrent laryngeal nerve injury leading to vocal cord paresis, which is suggested by hoarseness and the development of stridor requiring re-intubation. Ultimately she will require direct laryngoscopy for visualization of the vocal folds to assess for paralysis.

(A) While accidental removal of the parathyroids may lead to hypocalcemia, this effect would not be expected so rapidly after surgery and would not be expected to result in hoarseness or stridor. (B) Infection with *Haemophilus influenzae* may lead to stridor in pediatric patients, but this individual's history of recent surgical intervention makes acute infection less likely. (D) There was no report of swelling at the surgical site, so a hematoma would be unlikely. (E) Anaphylaxis refers to immediate hypersensitivity to a foreign antigen. While anaphylaxis secondary to anesthesia medications is possible, it would have been expected to occur earlier in the patient's time course.



A 46-year-old man with a lifelong history of asthma develops worsening shortness of breath and a productive cough over the past 2 weeks. Laboratory samples are drawn in the Emergency Department and are shown below.

|                                           |                         |
|-------------------------------------------|-------------------------|
| Hemoglobin                                | 13.2 g/dL               |
| Mean corpuscular volume                   | 89 fL                   |
| Mean corpuscular hemoglobin               | 31.0 pg                 |
| Mean corpuscular hemoglobin concentration | 34.5 g/dL               |
| Red cell distribution width               | 14.6 fL                 |
| Leukocyte count                           | 6,700/mm <sup>3</sup>   |
| Neutrophils                               | 51%                     |
| Lymphocytes                               | 24%                     |
| Eosinophils                               | 22%                     |
| Basophils                                 | 3%                      |
| Platelets                                 | 250,000/mm <sup>3</sup> |

A chest x-ray shows parenchymal infiltrates and evidence of bronchial dilation.

What is the most likely cause of his pneumonia?

- (A) *Mycoplasma pneumoniae*
- (B) *Streptococcus pneumoniae*
- (C) *Klebsiella pneumoniae*
- (D) *Aspergillus*
- (E) Acute HIV infection

**The answer is D: *Aspergillus*.** Allergic bronchopulmonary aspergillosis is a hypersensitivity reaction found most frequently among individuals with asthma or cystic fibrosis. Eosinophilic pneumonia is one manifestation of aspergillosis in such individuals. *Aspergillus* may be cultured from the sputum of such patients and septated hyphae may be seen under microscopic examination. Chest radiography will show infiltrates, atelectasis, and signs of bronchiectasis.

(A, B) *Mycoplasma* and *S. pneumoniae* are common causes of pneumonia, but would not produce eosinophilia. (C) *Klebsiella pneumoniae* is a common cause of pneumonia among individuals who have aspirated. (E) While acute onset of HIV may present with respiratory tract symptoms, it is not commonly associated with peripheral eosinophilia and radiographic findings suggestive of pneumonia.

9

A 22-year-old man presents with abdominal pain for the last 4 years. The patient reports that the pain improves with defecation. He denies nausea, vomiting, diarrhea, and weight loss. The patient has an extensive family history of colon cancer (several of whom were diagnosed before the age of 40). Colonoscopy reveals hundreds of polyps in the colon and rectum.

Which is the risk of colon cancer in this patient's lifetime?

- (A) 1%
- (B) 10%
- (C) 25%
- (D) 50%
- (E) 95%
- (F) 100%

**The answer is F: 100%.** This patient has familial adenomatous polyposis (FAP), an autosomal dominant disease in which patients typically have a first-degree relative with early onset colon cancer. Patients diagnosed with FAP should be offered total proctocolectomy at the time of diagnosis since the vast majority will develop colon cancer at the age of 45 and 100% will develop colon cancer in their lifetime. FAP patients should also get routine surveillance upper GI endoscopies as they are at an increased risk for gastric and duodenal carcinomas.

- 10** A 24-year-old man presents to the hospital after a near drowning. He has a history of a seizure disorder and experienced a seizure while swimming in his pool. He is currently alert but having difficulty breathing. His temperature is 37.3°C, blood pressure is 110/72 mmHg, heart rate is 134 beats per minute, and respiratory rate is 32 breaths per minute. He has no jugular venous distention, and other than being tachypneic, he has a normal physical examination. An arterial blood gas shows a  $\text{PaO}_2$  of 85 mmHg on supplemental oxygen with a face mask set to a fraction of inspired oxygen of 50%. A chest x-ray is ordered and shows bilateral infiltrates.

Which of the following is the correct diagnosis?

- (A) Heart failure
- (B) Central hypoventilation
- (C) Acute respiratory distress syndrome (ARDS)
- (D) Aspiration pneumonitis

**The answer is C: Acute respiratory distress syndrome (ARDS).** This patient meets criteria for ARDS: he has bilateral infiltrates on chest x-ray, a  $\text{PaO}_2/\text{FiO}_2$  ratio  $<200$ , and pulmonary edema that cannot be explained by heart failure (neck veins not distended). (A) Whereas ARDS is a potential complication of near drowning, heart failure is not; in addition, the lack of jugular venous distention argues against heart failure. (B) This patient is tachypneic with positive chest x-ray findings; therefore, his hypoxemia is not from hypoventilation. (D) Aspiration pneumonitis and pneumonia can lead to ARDS; however, this patient currently meets the definition of ARDS, making this the better answer.

- 11** A 27-year-old medical student undergoes an ECG as part of a class demonstration. The results are depicted in *Figure 12-3*. He has no history of hypertension, diabetes, transient ischemic attacks, syncope, or heart failure. He does not smoke. He is currently not experiencing any symptoms.



**Figure 12-3**

What is the best next step in management?

- (A) Immediate transesophageal echocardiogram (TEE) and cardioversion
- (B) Immediate administration of heparin
- (C) Cardiology appointment for exercise stress testing
- (D) Endocrinology appointment for thyroid function testing
- (E) Echocardiogram, complete blood count, and basic metabolic panel

**The answer is E: Echocardiogram, complete blood count, and basic metabolic panel.** Given the patient's young age, asymptomatic status, and lack of risk factors, it is likely that he has lone atrial fibrillation. However, structural heart disease, electrolyte abnormalities, and hyperthyroidism must be ruled out first. (A) If the patient were symptomatic, TEE to rule out a blood clot (given the unknown duration of fibrillation) and cardioversion would be the appropriate next steps. (B) Anticoagulation may be used prior to cardioversion if that decision is made. Given the patient's CHADS2 score of 0, long-term anticoagulation is not necessary. (C) Exercise testing can be used to determine if ischemic heart disease is contributing to the atrial fibrillation (unlikely in this patient) or to evaluate rhythm response in asymptomatic athletes who cannot use  $\beta$ -blockers for sports eligibility. However, this would not be the next step in evaluation of this patient. (D) Thyroid function testing alone would be inadequate.



12 A 38-year-old woman with past medical history of HIV infection presents with an inability to ambulate, urinary and fecal incontinence, and selective mutism. She is not currently taking any medications. On examination, her pupils are equal, round, and reactive with no papilledema noted. Extraocular movements are intact. She is able to plantarflex her left foot but not her right foot. Skin examination is notable for extensive seborrheic dermatitis at her hairline. An MRI reveals peripherally enhancing lesions of her basal ganglia, frontal lobe, and cerebellum.

Which of the following is the most likely cause of her neural deficits?

- (A) CNS lymphoma
- (B) *Toxoplasma gondii* encephalitis
- (C) Herpes encephalitis
- (D) Progressive multifocal leukoencephalopathy
- (E) *Pneumocystis jirovecii* brain abscess

**The answer is B: *Toxoplasma gondii* encephalitis.** *Toxoplasma* encephalitis is an opportunistic infection in AIDS patients. It usually presents as multiple ring-enhancing lesions affecting the basal ganglia. (A) CNS lymphoma also

can present with ring-enhancing lesions, but solitary lesions and whole tumor enhancement is more common. (C, D) Herpes encephalitis and progressive multifocal leukoencephalopathy do not present as ring-enhancing lesions. (E) *Pneumocystis jirovecii* brain abscesses can also present as multiple ring-enhancing lesions and be difficult to distinguish from *Toxoplasma* encephalitis, but CNS *Pneumocystis jirovecii* infection is extremely rare.

13

A 52-year-old woman with a history of asthma since childhood presents to the Emergency Department with severe shortness of breath and wheezing. When speaking to the intake nurse, she is only able to say one to two words at a time due to her difficulty breathing. She has been using her albuterol rescue inhaler without any improvement in her symptoms. On physical examination, she appears very anxious with rapid shallow breaths and diffuse inspiratory wheezes. Vital signs are: blood pressure 118/68 mmHg, heart rate 120 beats per minute, respiratory rate 32 breaths per minute, and oxygen saturation of 81% on 6 L supplemental O<sub>2</sub> from a nonrebreather mask. A stat ABG is sent and shows a PaO<sub>2</sub> of 54 mmHg.

What is the best next step in management?

- (A) Chest x-ray
- (B) Emergent intubation
- (C) Repeat ABG
- (D) Offer reassurance and lorazepam
- (E) Trial of nebulized ipratropium and albuterol

**The answer is B: Emergent intubation.** This patient is in respiratory distress due to an asthma exacerbation. Her critically low pO<sub>2</sub> on ABG and her low O<sub>2</sub> saturation despite supplemental oxygen indicate that she is not sufficiently oxygenating on her own and has respiratory muscle fatigue. The best next step is thus emergency intubation. (A, C) Intubation should not be delayed by a chest x-ray or repeat ABG. (D) Hypoxemia would not be seen in panic disorder. (E) Ipratropium and albuterol are treatments of an acute asthma exacerbation; however, intubation should be the first priority.

14

A 69-year-old woman with metastatic breast cancer is brought in by her family with severe back pain. She states that her pain is 10/10 and that her current goals of care are to be comfortable and to enjoy time at home with her husband and children. She is alert and oriented and has full understanding of her condition and prognosis. Her eldest son, who is her durable power of attorney (DOA), is demanding that she continues radiation and chemotherapy for her metastatic cancer.

Which of the following is the best action in this situation?

- (A) Consult the hospital ethics committee
- (B) Proceed with radiation and chemotherapy since the son is her DOA
- (C) Give morphine intravenously and consult the palliative care team
- (D) Consult neurosurgery to evaluate for spinal surgery

**The answer is C: Give morphine intravenously and consult the palliative care team.** The patient in this vignette is still competent and able to make decisions. (B) Even though her son is the DOA, her wishes should still be followed. (A) Most answer choices that shift the responsibility to another physician or group (such as an ethics committee) is likely to be wrong on the test. (D) The patient desires to be at home with her family and therefore surgery is not a good answer choice.

- 15** A 77-year-old man is admitted to the hospital after an acute change in mental status during the previous day, which was following a mild upper respiratory infection. He has a longstanding history of type 2 diabetes and sometimes forgets to take his medications. Blood glucose on admission is 670 mg/dL, and over the course of the first hospital day his urine output is 3 L.

What additional finding would you expect to see in this patient?

- (A) Decreased serum osmolality
- (B) Metabolic acidosis
- (C) Ketones in the urine, but not in the blood
- (D) Severe volume depletion
- (E) Increased reflexes

**The answer is D: Severe volume depletion.** This patient is experiencing hyperosmolar hyperglycemic state (also called nonketotic hyperglycemia), a dangerous complication of type 2. It is defined as having a glucose >600 mg/dL and a serum osmolality >320 mOsm/kg. Patients will eventually progress to oliguria and prerenal azotemia, which is particularly concerning because many of these patients have underlying diabetic nephropathy. (A) The serum osmolality would be increased, not decreased, due to the loss of free water caused by osmotic diuresis associated with hyperglycemia and glycosuria. (B, C, E) Arterial pH is usually normal, serum ketones are few or absent, and reflexes are depressed. Mortality for this condition is up to 20%, and early fluid resuscitation is crucial.

- 16** A 71-year-old man is brought to the Emergency Department complaining of 2 hours of severe, tearing chest pain that radiates to his neck and back. His past medical history includes longstanding hypertension

and diabetes, for which he takes lisinopril, glipizide, and amlodipine. On examination, he is anxious, tachycardic, and his blood pressure is 176/88 mmHg in the right arm and 148/70 mmHg in the left arm. His lung examination is normal.

What other finding would you expect in this patient?

- (A) Jugular venous distension
- (B) Diffuse ST elevations on ECG
- (C) Extensive fluid collection surrounding the pancreas on CT
- (D) Early diastolic decrescendo murmur at the right sternal border
- (E) Reduced ejection fraction on transthoracic echocardiogram
- (F) Electrical alternans on ECG

**The answer is D: Early diastolic decrescendo murmur at the right sternal border.** An early diastolic decrescendo murmur is indicative of aortic regurgitation, which may be present in the case of an aortic dissection involving the aortic arch. This diagnosis is suggested by the tearing chest pain, history of hypertension, and mismatched blood pressure readings between his arms. (A) Jugular venous distention is indicative of heart failure, and aortic dissections can cause heart failure; however, it would cause left heart failure and there would be rales on lung examination. (B) Myocardial infarctions are a consequence of ascending aortic dissections that involve a coronary artery; however, the ST elevations would be in the territory of a coronary artery (and not diffuse as is seen in acute pericarditis). (C) Acute pancreatitis would not present with a blood pressure difference between the left and right arms. (E) There is no evidence of heart failure at this time, since the patient is maintaining an elevated blood pressure and has a normal lung examination. (F) Electrical alternans would indicate a significant pericardial effusion, which can happen with aortic dissections. However, a fluid collection large enough to cause electrical alternans would impair cardiac output and lead to cardiogenic shock, which this patient does not have.

17

A 29-year-old man is brought to the Emergency Department after suffering multiple stab wounds to his abdomen. He was found on the street actively bleeding. His blood pressure upon arrival was 82/50 mmHg. He received 4 L of IV fluids and 4 units of packed red blood cells. He is sent to the operating room and is then transferred to the intensive care unit. His current vitals show a blood pressure of 110/76 mmHg and a heart rate of 80 beats per minute. A further history is obtained, and he has no medical problems and takes no

medications. His laboratory values 24 hours after initial presentation are shown below.

|                     |           |
|---------------------|-----------|
| Hemoglobin          | 8.7 g/dL  |
| Blood urea nitrogen | 38 mg/dL  |
| Creatinine          | 2.8 mg/dL |

If a urinalysis is performed, which of the following would most likely be seen?

- (A) Red blood cell casts
- (B) White blood cell casts
- (C) Waxy casts
- (D) Muddy brown casts
- (E) Eosinophils

**The answer is D: Muddy brown casts.** This patient suffered from hypovolemic shock due to hemorrhage. As a result of hypoperfusion to his kidneys, he developed acute tubular necrosis (ATN), which is the most common form of acute kidney injury (AKI) in hospitalized patients. Muddy brown casts on urinalysis is a sensitive finding for ATN. (A) RBC casts would indicate glomerulonephritis. (B) WBC casts are typically seen in acute interstitial nephritis, pyelonephritis, and glomerulonephritis. (C) Waxy casts are seen in advanced chronic kidney disease. (E) Eosinophils are commonly seen in acute interstitial nephritis or with cholesterol emboli causing acute renal failure.



18 A 25-year-old woman is evaluated for daily nosebleeds for the last year. The nosebleeds often begin in the morning upon awakening and are easily controlled. She states that she also had daily nosebleeds as a child. She denies any recent illness, fever, chills, or weight loss. She takes no medications. Her mother and sister also have chronic nosebleeds. Her laboratory results are shown below.

|                                       |                         |
|---------------------------------------|-------------------------|
| Hemoglobin                            | 13.0 g/dL               |
| Leukocyte count                       | 6,000/mm <sup>3</sup>   |
| Platelets                             | 250,000/mm <sup>3</sup> |
| Prothrombin time                      | 15 seconds              |
| Activated partial thromboplastin time | 45 seconds              |
| Bleeding time                         | 12 minutes              |



The patient is given the first-line treatment for her disease.

What is this medication's composition and/or mechanism of action?

- (A) Repletion of factor VIII and von Willebrand factor
- (B) Repletion of factors II, V, VII, IX, X, and XI
- (C) Inhibition of carboxylation via  $\gamma$ -glutamyl carboxylase
- (D) Release of von Willebrand factor from endothelial cells

**The answer is D: Release of von Willebrand factor from endothelial cells.** This patient likely has von Willebrand disease (vWD). Desmopressin is the first-line treatment of vWD, and works by stimulating the release of vWF from endothelial cells via the V2 receptor. (A) Cryoprecipitate contains factor VIII and fibrinogen with small amounts of vWF and factor XIII. Although it is possible to treat vWD or Hemophilia A with cryoprecipitate, it is typically reserved for cases refractory to desmopressin. (B, C) Fresh frozen plasma is not typically used for vWD, and warfarin would only exacerbate this patient's coagulopathy.



A 65-year-old man with a history of diet-controlled diabetes mellitus, hypertension, and hyperlipidemia presents to the Emergency Department with chest pain and is admitted for a STEMI. His only medication is lisinopril. His metabolic panel on admission is as follows.

|                     |           |
|---------------------|-----------|
| Sodium              | 138 mEq/L |
| Potassium           | 3.8 mEq/L |
| Chloride            | 102 mEq/L |
| Bicarbonate         | 24 mEq/L  |
| Blood urea nitrogen | 15 mg/dL  |
| Creatinine          | 1.0 mg/dL |
| Glucose             | 110 mg/dL |

He undergoes percutaneous coronary intervention with placement of a stent. About 36 hours later, he complains of decreased urination. His vitals show a temperature of 37°C, a blood pressure of 120/80 mmHg, and a pulse of 75/min. His cardiac, lung, and skin examinations are normal. Mucous membranes are moist. More laboratory values are sent, which show a blood urea nitrogen (BUN) of 30 mg/dL and a creatinine of 1.7 mg/dL. A renal ultrasound shows no hydronephrosis.

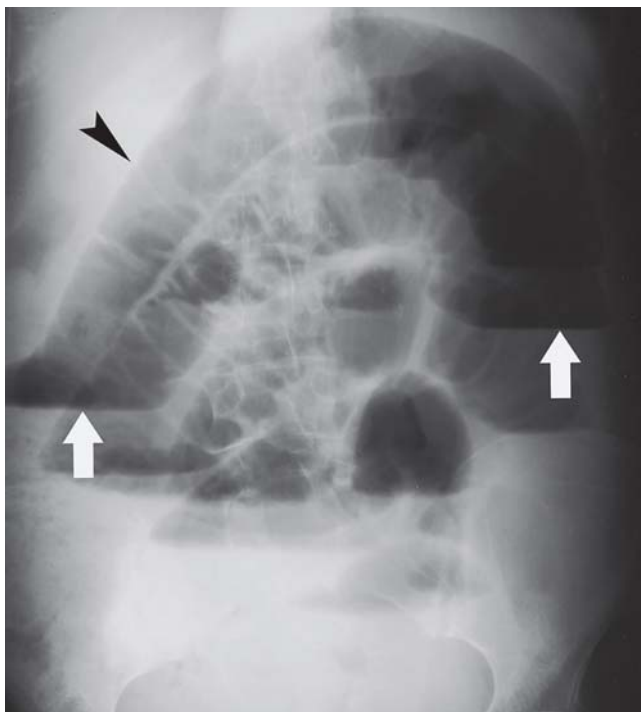
Which of the following urinalysis results are most consistent with this patient's diagnosis? (Note: SG is specific gravity, Neg is negative, Pos is positive, W is white blood cell, R is red blood cell.)

|     | SG    | Protein | Glucose | Ketones | Nitrites | Cells     | Other             |
|-----|-------|---------|---------|---------|----------|-----------|-------------------|
| (A) | 1.042 | Neg     | Neg     | Neg     | Neg      | 1 W, 2 R  | Hyaline casts     |
| (B) | 1.010 | Neg     | Neg     | Neg     | Neg      | 1 W, 2 R  |                   |
| (C) | 1.020 | Neg     | Neg     | Neg     | Pos      | 30 W, 5 R |                   |
| (D) | 1.015 | 2+      | 1+      | 2+      | Neg      | 4 W, 1 R  |                   |
| (E) | 1.010 | Trace   | Neg     | Neg     | Neg      | 4 W, 1 R  | Muddy brown casts |
| (F) | 1.010 | Neg     | Neg     | Neg     | Neg      | 4 W, 1 R  | R casts, W casts  |
| (G) | 1.015 | Neg     | Neg     | Neg     | Neg      | 50 W, 1 R | W casts           |

**The answer is E: Specific gravity 1.010, trace protein, negative glucose, negative ketones, negative nitrites, 4 WBCs, 1 RBC, muddy brown casts.** This patient has AKI as evidenced by his abrupt increase in serum BUN and creatinine values. ATN is the most common form of intrarenal disease that causes AKI in hospitalized patients and is the likely etiology in this patient. Contrast agents used in coronary angiography are known nephrotoxins, which typically presents within 24 to 48 hours after exposure and is the likely etiology in this patient. Cholesterol crystal embolization typically presents after 48 hours and is thus less likely but may also cause ATN. (A) This is the urinalysis of a patient with dehydration. Although profound hypotension can progress to ATN, this patient is euvolemic by vital signs and examination. (B) This is a normal urinalysis. (C) This is consistent with a urinary tract infection (UTI). (D) This is a possible urinalysis in a patient with diabetes. (F) This is most consistent with acute glomerulonephritis given the RBC casts and dysmorphic RBCs. (G) Sterile pyuria may be present in acute interstitial nephritis.



A 66-year-old woman with a history of multiple abdominal surgeries presents with nausea, vomiting, and abdominal pain. Abdominal x-ray is shown in *Figure 12-4*.



**Figure 12-4**

Which of the following is the likely etiology of this patient's disease?

- (A) Stricture formation
- (B) Perforation
- (C) Adhesion formation
- (D) Inflammation

**The answer is C: Adhesion formation.** This patient is presenting with a small bowel obstruction, which is indicated by the air–fluid levels on x-ray. The most common cause of small bowel obstruction in patients with a history of abdominal surgery is adhesion formation. (A, B, D) These other choices are less common causes of small bowel obstruction.

**21**

A 55-year-old man presents to his primary care physician for a routine physical examination at his wife's insistence. He has a medical history of benign prostatic hyperplasia and depression, but has refused medications previously. Intake vitals show a blood pressure of 148/92 mmHg, a heart rate of 78 beats per minute, and a respiratory rate of 12 breaths per minute.

He is counseled about lifestyle changes and scheduled to follow-up. His elevated blood pressure is confirmed at two more office visits, and screening examinations and tests do not indicate any end-organ damage.

What is the next step in managing his hypertension?

- (A) No intervention required, since the patient is asymptomatic
- (B) Begin a low-dose ACE inhibitor and calcium channel blocker
- (C) Instruct the patient to return in 1 month for repeat blood pressure measurement
- (D) Begin an  $\alpha$ -blocker
- (E) Begin a  $\beta$ -blocker
- (F) Immediate IV hydralazine

**The answer is D: Begin an  $\alpha$ -blocker.** (A, C) The patient can now be diagnosed with hypertension, since his high blood pressure has been confirmed at three visits. Given that his blood pressure has remained high despite lifestyle changes, it is now appropriate to begin pharmacologic therapy. Achieving a specific blood pressure target is often more important than the specific agent selected; however, there are some reasons for choosing a specific agent. An  $\alpha$ -blocker would have the benefit of reducing blood pressure while also treating his benign prostatic hyperplasia. Other diseases that benefit from selecting a specific antihypertensive agent include diabetes (ACE inhibitor, ARB), heart failure or post-MI (ACE inhibitor, ARB,  $\beta$ -blocker, aldosterone antagonist), atrial fibrillation ( $\beta$ -blocker, calcium channel blocker), essential tremor ( $\beta$ -blocker), Raynaud phenomenon (calcium channel blocker), osteoporosis (thiazide diuretic, which increases calcium reabsorption), and hyperthyroidism ( $\beta$ -blocker). (B) Starting therapy with two drugs is appropriate when the baseline blood pressure is  $>160/100$  mmHg. (E) Starting a  $\beta$ -blocker would be unwise, given his history of depression. (F) The patient does not meet the definition of hypertensive urgency or emergency and does not need immediate blood pressure reduction.



A 55-year-old woman with known ulcerative colitis is admitted to the hospital for intractable diarrhea. She has had eight to ten episodes per day for the past 2 days, along with a fever of  $39.1^{\circ}\text{C}$ . She is typically on 5-ASA for maintenance, which is prescribed by her gastroenterologist in South America, where she is from. She has never had a colonoscopy. In the hospital, she fails to improve with IV methylprednisolone.

What is this patient's contraindication for starting infliximab?

- (A) Presumed dehydration from severe diarrhea
- (B) Interaction with 5-ASA
- (C) No documented PPD test
- (D) No documented colonoscopy
- (E) Symptoms are not severe enough to indicate infliximab use

**The answer is C: No documented PPD test.** Severe ulcerative colitis flares are characterized by >6 bowel movements per day and systemic symptoms. If a severe flare has failed IV steroids, the next step would be an anti-TNF $\alpha$  agent such as infliximab. However, this drug carries the risk of reactivation TB and requires a documented negative PPD prior to use. (A, B) These are not contraindications to infliximab use. (E) A valid alternative in this case would be cyclosporine A, as additional treatment is required for this severe flare. (D) Infliximab has no correlation with colon cancer, although it does carry a slightly increased risk of lymphoma.

23

A 38-year-old woman presents to the office for a routine evaluation. She has no current complaints or current medical problems. However, she states that as a child she was ill with “aching joints” and “rashes on her arms” and was treated with “some antibiotic for a long time.” She is not on any medications and has no known allergies. On examination, her vitals are normal. On cardiovascular examination, she has a faint mid-diastolic murmur heard best at the apex. The rest of her examination is normal. She is scheduled to undergo a dental procedure next week.

What is the most appropriate step in management?

- (A) Oral amoxicillin 30 minutes before the procedure
- (B) Oral amoxicillin 2 hours before the procedure
- (C) IV ampicillin 30 minutes before the procedure
- (D) IV ampicillin 2 hours before the procedure
- (E) No prophylaxis needed

**The answer is E: No prophylaxis needed.** Prophylaxis for infective endocarditis is recommended only for patients at the highest risk of developing a serious complication if infective endocarditis were to occur. These include patients with prosthetic heart valves, a history of infective endocarditis, a cyanotic congenital cardiac disease that is unrepaired, or patients with heart transplants that also have valvular disease. (A, C) Appropriate prophylaxis for these patients would be oral amoxicillin 30 to 60 minutes prior to the procedure, or IV ampicillin for patients who cannot tolerate oral medications. This patient likely had rheumatic fever as a child and has mild mitral stenosis as a result; however, this is not an indication for antibiotic prophylaxis before dental procedures.

24

An 83-year-old man with a history of hypertension, diabetes, and prostate cancer presents to the Emergency Department complaining of 4 days of back pain worsened with coughing. Associated symptoms include lower-extremity numbness. On further questioning, the patient reveals three episodes of urinary incontinence and one episode of losing bowel control. Physical examination is notable for hyper-reflexia of the lower extremities and decreased sphincter tone.

Where is the most likely lesion in this patient?

- (A) Brain stem
- (B) Cervical spine
- (C) Thoracic spine
- (D) Lumbar spine
- (E) Sciatic nerve

**The answer is D: Lumbar spine.** Spinal cord compression is a neurologic emergency. The most common site of bony metastasis in prostate cancer is the spine, and the lumbar spine is most frequently affected. Patients can present with back pain, bowel/bladder incontinence, erectile dysfunction, saddle anesthesia, lower-extremity sensory deficits and weakness, and upper motor neuron signs below the lesion. MRI is the diagnostic test of choice. High-dose dexamethasone should be started immediately, but many patients ultimately require surgical decompression.

**25** A 44-year-old man presents for a routine health maintenance visit. He has no past medical history. He smokes half a pack of cigarettes daily and does not consume alcohol. His diet consists of fast food on a regular basis. His mother has diabetes and his father has high cholesterol. The patient has a heart rate of 72 beats per minute and a blood pressure of 138/74 mmHg. He has a BMI of 32 kg/m<sup>2</sup>. Laboratory results are shown below.

|                   |           |
|-------------------|-----------|
| Total cholesterol | 198 mg/dL |
| HDL               | 54 mg/dL  |
| LDL               | 125 mg/dL |
| Triglycerides     | 150 mg/dL |
| Fasting glucose   | 130 mg/dL |

A repeat fasting glucose 2 weeks later shows a glucose of 134 mg/dL.

Aside from starting the patient on metformin, what is the most appropriate next step in management?

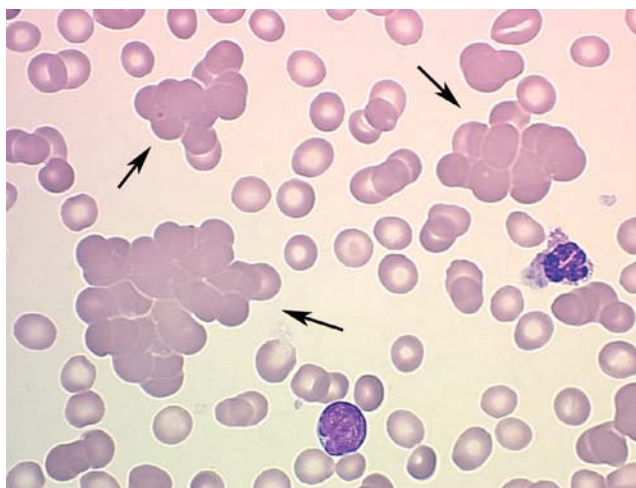
- (A) Lifestyle modification only
- (B) Fish oil supplementation
- (C) Oral atorvastatin
- (D) Oral niacin
- (E) Oral lisinopril

**The answer is C: Oral atorvastatin.** Guidelines for initiating lipid-lowering therapy with a statin include those with clinically significant atherosclerotic disease (including myocardial infarction, stroke, coronary revascularization), LDL >190 mg/dL, diabetics between the ages of 40 to 75, and those with a 10-year risk of cardiovascular disease >7.5% (ACC/AHA opinion). This patient has two fasting blood glucose levels  $\geq 126$  mg/dL, making the diagnosis of diabetes. As such, he should begin a statin along with medications to control his blood glucose.

26

A 68-year-old man complains of cold blue hands. He first noticed a color change in the fall and reports that it has persisted through the winter. Further questioning reveals that he has been experiencing drenching night sweats the past few months and intermittent fevers. His wife notes that he has lost about 10 kg from his usual 80 kg weight at that time. She also notes that he has become more tired than usual and no longer wants to play tennis with their friends. Both his spleen and liver are palpable on examination. Laboratory results as well as his peripheral blood smear (*Figure 12-5*) are shown below.

|                 |                                      |
|-----------------|--------------------------------------|
| Hemoglobin      | 9.4 g/dL                             |
| Leukocyte count | 36,100/mm <sup>3</sup>               |
| Platelets       | 140,000/mm <sup>3</sup>              |
| LDH             | 410 U/L (normal range 140–280 U/L)   |
| Haptoglobin     | 27 mg/dL (normal range 45–165 mg/dL) |



**Figure 12-5**

What is the most likely cause of his chief complaint?

- (A) Raynaud phenomenon
- (B) Cold agglutinin disease
- (C) Thromboangiitis obliterans
- (D) Connective tissue disorder
- (E) Hashimoto thyroiditis

**The answer is B: Cold agglutinin disease.** This patient is presenting with new onset leukemia, most likely chronic lymphocytic leukemia (CLL) given his age. In addition he is complaining of acrocyanosis. Individuals with CLL may develop cold agglutinin disease, which refers to the presence of IgM antibodies that target red blood cells and lead to autoimmune hemolytic anemia. Acrocyanosis may also result from agglutination of red blood cells in the small vessels of the hands and is most pronounced in cold climates.

(A) Raynaud phenomenon is vasoconstriction of the vessels in the hands due to cold temperature or emotional stress. It is not known to be associated with leukemia. (C) Thromboangiitis obliterans or Buerger disease is an inflammatory disease of small- to medium-sized vessels that classically affects smokers and leads to digital ischemia. (D) Connective tissue disorders such as Ehlers–Danlos and systemic sclerosis are also associated with digital ischemia; however, these are unlikely to coincide acutely with new-onset leukemia. (E) While Hashimoto thyroiditis may be associated with cold intolerance, it does not necessarily worsen with cold weather. It is not known to be associated with leukemia.

**27** A 15-year-old boy is brought in by his mother with a 3-day history of dark urine. The patient feels well but reports having a severe sore throat 3 weeks ago that resolved on its own. Physical examination reveals a blood pressure of 142/88 mmHg and periorbital edema.

Which of the following is the underlying mechanism for this patient's disease?

- (A) Basement membrane thickening
- (B) Type III hypersensitivity reaction
- (C) Foot process effacement
- (D) Mesangial proliferation

**The answer is B: Type III hypersensitivity reaction.** This patient is presenting with history (previous sore throat) and signs (hypertension, dark urine) consistent with poststreptococcal glomerulonephritis (PSGN). In PSGN, circulating antibody–antigen immune complexes deposit in the glomeruli of the kidneys. The mechanism of disease is a type III hypersensitivity reaction in which immune complexes form in the blood and deposit in tissues, activating the complement cascade and other immunologic damage. Type II



hypersensitivity reactions occur due to antibodies directed at fixed antigens (not circulating in the blood stream). An example is rheumatic fever, in which antibodies previously formed will cross-react with myocardial cell antigens.

**28**

A 63-year-old woman presents to the hospital with cough and shortness of breath. She has not been to the doctor in years and has no medical history. Her symptoms have been present for the past few years, but have been unbearable over the last week when she developed a worsening cough that was productive of yellow sputum. She cannot walk 50 feet without becoming exceedingly short of breath. She drinks alcohol moderately and has a 40 pack-year smoking history. On examination, her temperature is 38.1°C, blood pressure is 108/62 mmHg, heart rate is 102 beats per minute, respiratory rate is 28 breaths per minute, and oxygen saturation is 91%. Her examination is notable for mild jugular venous distention, distant heart and breath sounds, and scattered wheezes and rhonchi.

Which of the following is NOT recommended as therapy at this time?

- (A) Furosemide
- (B) Methylprednisolone
- (C) Albuterol
- (D) Levofloxacin
- (E) Ipratropium

**The answer is A: Furosemide.** This patient is presenting with undiagnosed COPD and is having an acute exacerbation. The treatment for an acute exacerbation is oxygenation (goal oxygen saturation of 90% to 93% if she is a chronic CO<sub>2</sub> retainer), ipratropium, and steroids. Albuterol is less important but may also be helpful. Furosemide is an important treatment in congestive heart failure. Although this patient could have right heart failure (cor pulmonale) from COPD and chronic hypoxemia, this is not the immediate concern. In addition, patients with pulmonary hypertension have a narrow range of ideal fluid balance to produce a satisfactory output from the right ventricle; therefore, diuresis can be dangerous if the patient is not truly fluid overloaded.

**29**

A 55-year-old man presents to the Emergency Department complaining of chest pain radiating to his left shoulder. ECG reveals ST segment elevation in leads II, III, and aVF. Serum troponins are elevated. Vital signs show a temperature of 37°C, a blood pressure of 101/63 mmHg, a heart rate of 65 beats per minute, and a respiratory rate of 16 breaths per minute. Physical examination reveals diaphoresis, elevated jugular venous pressure (JVP), and a late systolic murmur. Lungs are clear to auscultation.

Which of the following can safely be used to treat the patient's condition without risk of worsening his hemodynamic status?

- (A) IV fluids
- (B) Morphine
- (C)  $\beta$ -blockers
- (D) Furosemide
- (E) Aspirin

**The answer is E: Aspirin.** The patient has had an inferior wall myocardial infarction (MI) with evidence of right heart failure. Management of right heart MI involves optimization of preload, afterload, and contractility. (A) IV fluids must be used with caution for right heart failure since they can overload the damaged right ventricle. (B, D) Opioids and diuretics decrease preload and can decrease cardiac output. (C)  $\beta$ -blockers will decrease cardiac contractility and may further decrease the patient's blood pressure, increasing his risk of shock.

30

A 52-year-old man is brought to the Emergency Department for sudden onset of chest pain that developed 30 minutes ago. He was sitting at home watching TV when he developed the chest pain. He had upper respiratory symptoms 1 week ago that resolved with supportive treatment. He has a long history of hypertension and hyperlipidemia. His current medications include lisinopril and atorvastatin. He has a temperature of 37.3°C, a blood pressure of 155/88 mmHg, a heart rate of 104 beats per minute, and a respiratory rate of 16 breaths per minute. He is anxious on examination, and has an S4 on cardiac examination. His lungs are clear to auscultation bilaterally. An initial ECG is performed (*Figure 12-6*), and troponins are drawn and found to be negative.



Figure 12-6

What is the most likely diagnosis?

- (A) STEMI
- (B) NSTEMI
- (C) Aortic dissection
- (D) Pericarditis

**The answer is A: STEMI.** This patient presents with risk factors and symptoms concerning for a myocardial infarction. The ECG shows ST elevations in the inferior leads (II, III, aVF). Troponins may not be elevated until 3 to 5 hours after the myocardial tissue infarcts, and they may remain elevated for up to 14 days. Troponins should be drawn on admission and repeated every 8 hours for 24 hours. In this case, the initial troponin test is negative given that his pain only occurred 30 minutes ago. The ECG shows ST elevations that confirm that the diagnosis is STEMI. (B) An NSTEMI would not show ST elevations on ECG. (C) An aortic dissection may lead to a myocardial infarction if the dissection involves a coronary artery, but there are no other findings to suggest this as the cause of this patient's infarction. (D) Pericarditis would show diffuse ST elevations in all leads.



31 A 21-year-old man presents to the Emergency Department complaining of nausea, vomiting, and severe headache for the past 24 hours, which increases in severity while lying flat. On examination, his temperature is 38.5°C, blood pressure is 140/85 mmHg, and heart rate is 105 beats per minute. His neck is stiff. Lumbar puncture is performed but the results are pending.

What is the most appropriate course of action at this time?

- (A) Begin ceftriaxone
- (B) Wait for the cerebrospinal fluid (CSF) analysis before beginning treatment
- (C) Begin ceftriaxone, vancomycin, and acyclovir
- (D) Begin ceftriaxone, vancomycin, and ampicillin
- (E) CT scan

**The answer is C: Begin ceftriaxone, vancomycin, and acyclovir.** This patient's presentation is most consistent with meningitis, and bacterial and viral causes are most concerning in this patient given the acute presentation. (B) Empiric antibiotics should be started immediately after the lumbar puncture is performed. Ceftriaxone and vancomycin are appropriate coverage for *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*, the most common pathogens involved in patients aged 3 months to 50 years of age. Acyclovir is an appropriate addition if a viral etiology such as HSV is suspected. (A, D) Ceftriaxone alone would not cover resistant *S. pneumoniae* strains, and ampicillin is unnecessary given the low incidence

of *Listeria meningitis* in patients between the ages of 3 months and 50 years. (E) A CT scan of the head may be performed before a lumbar puncture if there is a suspicion for a space-occupying lesion, but the lumbar puncture has already been performed.

**32** A 65-year-old Russian man presents to the Emergency Department at 2 AM complaining of chest pain. No one is available to translate at this time. His wife produces limited records from an outside hospital from an admission 6 weeks ago, which includes an ECG performed at that time. On examination, his temperature is 37.0°C, blood pressure is 140/85 mmHg, and heart rate is 95 beats per minute. He is mildly diaphoretic, and his apical impulse is displaced to the left of the midclavicular line. An S3 is heard on auscultation. He has no jugular venous distention or lower-extremity edema. A 12-lead ECG is performed and shows ST elevations in the anterior leads, which is unchanged from the ECG performed 6 weeks ago from the outside hospital.

What was the most likely diagnosis made during the patient's admission to the outside hospital 6 weeks ago?

- (A) Pericarditis
- (B) Interventricular septal rupture
- (C) ST elevation myocardial infarction
- (D) Myocarditis
- (E) Congestive heart failure exacerbation

**The answer is C: ST elevation myocardial infarction.** This patient most likely presents with a left ventricular aneurysm, which is a late complication of ST elevation myocardial infarction (STEMI). Left ventricular aneurysms typically present 2 weeks to several months after an MI. Physical examination may reveal cardiac enlargement with a displaced apical impulse and an S3, indicating blood flow into a dilated ventricular chamber. ST elevations may persist from the original myocardial infarction, as evidenced on this patient's serial ECGs. (A) Postinfarct pericarditis presents with pleuritic chest pain, fever, and pericardial friction rub on examination within 24 hours of the infarction. ECGs may show diffuse ST elevation, but would not localize to a vascular territory such as in this patient. Dressler syndrome could present 6 weeks after infarction but signs of pericarditis (as above) should be present. (B) Interventricular septal rupture is a severe complication of MI, and often presents with shock and signs of cardiac tamponade. (D) Myocarditis is typically due to a viral illness and would likely be associated with fever and signs of congestive heart failure, which are absent in this patient. (E) The patient does not have jugular venous distention or lower-extremity edema, and the previous ECG showed ST elevations.

33

A 72-year-old woman with hypertension and hyperlipidemia presents to the clinic with a primary complaint of constipation. Her medications include a “water pill,” a statin, and a daily multivitamin. Her laboratory tests demonstrate the following.

|                             |                |
|-----------------------------|----------------|
| Sodium                      | 134 mEq/L      |
| Potassium                   | 3.8 mEq/L      |
| Chloride                    | 100 mEq/L      |
| Bicarbonate                 | 24 mEq/L       |
| Blood urea nitrogen         | 14 mg/dL       |
| Creatinine                  | 0.9 mg/dL      |
| Glucose                     | 108 mg/dL      |
| Calcium                     | 10.7 mg/dL     |
| Parathyroid hormone         | 9.5 pg/mL      |
| Thyroid-stimulating hormone | 3.2 $\mu$ U/mL |

What is most likely responsible for the patient’s complaint and laboratory findings?

- (A) Hydrochlorothiazide
- (B) Primary hyperparathyroidism
- (C) Secondary hyperparathyroidism
- (D) Malignancy
- (E) Hypervitaminosis D

**The answer is A: Hydrochlorothiazide.** Thiazide diuretics are the most likely cause of this patient’s elevated calcium levels; they also cause hyponatremia, hypercalcemia, and hyperglycemia, which are seen in this patient. (B, C) Both primary and secondary hyperparathyroidism would have an elevated parathyroid hormone (PTH); secondary hyperparathyroidism would have hypocalcemia. (D) Malignancy will generally produce more elevated calcium levels. (E) A typical multivitamin would not cause excessive vitamin D levels.

34

A 28-year-old woman presents for a routine clinic appointment. She has no past medical history and does not take any medications. On examination, a thyroid nodule is palpated. Laboratory studies show a

TSH of 1.4  $\mu\text{U/mL}$ . An ultrasound is performed and a single nodule is visualized with a width of 1.2 cm.

What is the next best step in management?

- (A) Reassurance and follow-up in 1 month
- (B) Treat with propylthiouracil
- (C) Radioactive iodine ablation
- (D) Radioactive iodine uptake study
- (E) Fine needle aspiration biopsy
- (F) Surgical excision

**The answer is E: Fine needle aspiration biopsy.** Nonfunctioning thyroid nodules (indicated by a normal or high TSH) should be biopsied to rule out malignancy. (A) Reassurance is only appropriate after malignancy is excluded. (B) Medical management with methimazole or propylthiouracil is an option for someone with hyperthyroidism due to Graves disease. (C) Radioactive ablation is the definitive treatment for Graves disease. (D) A radioactive iodine uptake study (scintigraphy) would be helpful to confirm a hyperfunctioning nodule if the TSH were low. If this had been the case, a fine needle aspiration biopsy would not have been necessary. (F) Surgery is too invasive at this stage of the workup but may be performed if the biopsy results are suspicious or confirm malignancy.

**35** A 40-year-old man comes to the cardiology clinic for a follow-up visit regarding his complete heart block. He recently had a pacemaker placed, and states that he is doing well. When you shake his hand, you notice that the patient has difficulty releasing his grip, and upon questioning he seems to have significant difficulty with concentration. His past surgical history is significant for bilateral cataract surgery.

What further testing should be done to confirm this man's additional diagnosis?

- (A) Muscle biopsy
- (B) Genetic sequencing for repeat expansions
- (C) Serum CK level
- (D) Temporal artery biopsy
- (E) No further testing needed

**The answer is E: No further testing needed.** Myotonic dystrophy is an autosomal dominant disease that affects multiple systems, producing myotonia (delayed relaxation of skeletal muscle), muscle weakness, cardiac conduction abnormalities, insulin resistance, and cataracts. Myotonic dystrophy is largely a clinical diagnosis, especially with such a characteristic constellation of symptoms/signs. (B) Genetic testing to diagnose specific variants is possible,

but not required. Therefore, no further testing is needed. (A) Muscle biopsy may show some abnormalities but is not a very useful test. (C) Serum CK will be mildly elevated but is nonspecific. (D) Temporal artery biopsy is an important diagnostic step in temporal (giant cell) arteritis.



A patient presents to his primary care physician for medical clearance prior to cataract surgery. His laboratory work reveals the following.

|                         |                         |
|-------------------------|-------------------------|
| Hemoglobin              | 13 g/dL                 |
| Mean corpuscular volume | 92 fL                   |
| Leukocyte count         | 5,000/mm <sup>3</sup>   |
| Neutrophils             | 15%                     |
| Lymphocytes             | 75%                     |
| Monocytes               | 5%                      |
| Eosinophils             | 0%                      |
| Basophils               | 0%                      |
| Platelets               | 200,000/mm <sup>3</sup> |

Past laboratory values reveal an elevated ANCA and anti-glucose-6-phosphate. Physical examination reveals splenomegaly.

Which additional findings are likely to be found on further evaluation?

- (A) Malar rash
- (B) Oral thrush and axillary lymphadenopathy
- (C) Swan-neck deformities
- (D) Nephritis
- (E) Night sweats and dyspnea

**The answer is C: Swan-neck deformities.** This patient has Felty syndrome, characterized by neutropenia, splenomegaly, and rheumatoid arthritis. (A, D) Malar rash and nephritis are associated with systemic lupus erythematosus (SLE), which can also occasionally be associated with neutropenia, splenomegaly, ANCA, and anti-glucose-6-phosphate. However, this combination of findings is more likely to be found in Felty syndrome. (B) Oral thrush and axillary lymphadenopathy are findings associated

with HIV infection, which is not associated with autoantibodies. (E) Night sweats and dyspnea are associated with TB, which is also not associated with autoantibodies.

**37** A 32-year-old woman with a history of bipolar disorder presents with excessive urination and thirst for the last week. Desmopressin is administered and the urine osmolality does not change.

Which of the following is the treatment for this patient's condition?

- (A) Furosemide
- (B) Hydrochlorothiazide
- (C) Spironolactone
- (D) Vasopressin

**The answer is B: Hydrochlorothiazide.** This patient is suffering from *nephrogenic* diabetes insipidus, likely secondary to long-term lithium use for bipolar disorder. Nephrogenic diabetes insipidus is characterized by a defective renal response to antidiuretic hormone (ADH, also known as vasopressin), in contrast to *central* diabetes insipidus in which there are insufficient levels of ADH. The first-line treatment is hydrochlorothiazide, which causes increased excretion of sodium and water, thereby reducing the serum osmolality and eliminating volume excess.

**38** A 37-year-old man presents with skin changes and abdominal pain. The abdominal pain is not affected by meals, and he has noticed painful red lesions on his hands and feet. He reports that he recently went on a backpacking trip, where he was bit by many mosquitoes and a few ticks. On examination, the patient is febrile. There is an early diastolic murmur auscultated at the left upper sternal border, and there is significant tenderness to palpation in the patient's right upper quadrant of the abdomen. The following laboratory values were obtained.

|                            |         |
|----------------------------|---------|
| Aspartate aminotransferase | 206 U/L |
| Alanine aminotransferase   | 366 U/L |
| Alkaline phosphatase       | 110 U/L |



An echocardiogram shows the following (Figure 12-7).

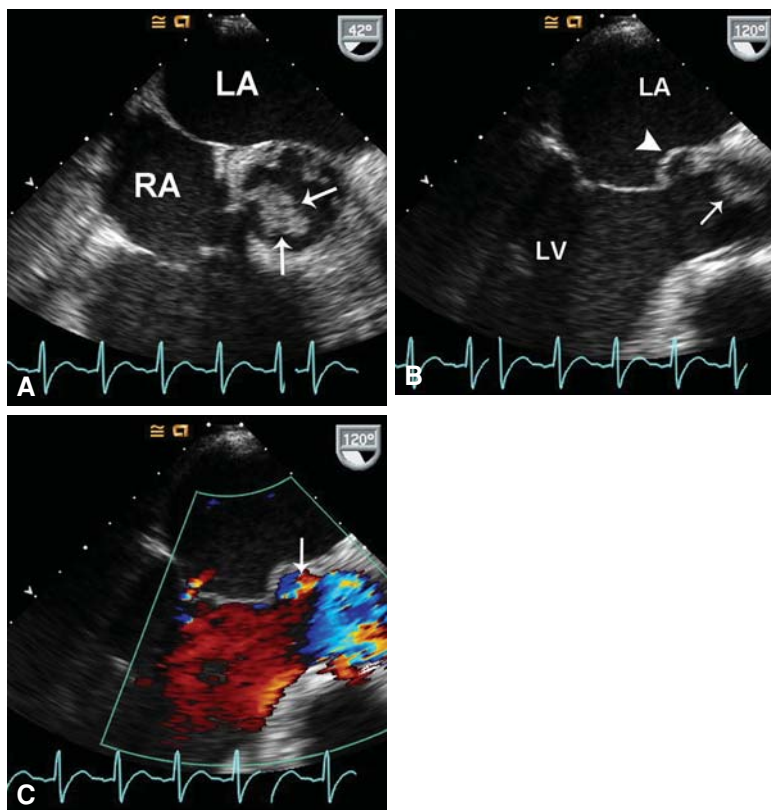


Figure 12-7

Which of the following organisms is likely responsible?

- (A) *Borrelia burgdorferi*
- (B) *Ehrlichia chaffeensis*
- (C) *Coxiella burnetii*
- (D) *Francisella tularensis*
- (E) *Streptococcus pneumoniae*
- (F) *Yersinia pestis*
- (G) *Babesia microti*
- (H) *Rickettsia rickettsii*
- (I) *Neisseria meningitidis*
- (J) Parvovirus B<sub>19</sub>

**The answer is C: *Coxiella burnetii*.** This bacterial species is responsible for Q fever, a zoonotic infection that can be asymptomatic or cause pneumonia, hepatitis, and/or endocarditis. This patient has hepatitis and endocarditis, the latter of which should raise suspicion for Q fever given his history of recent tick exposure. Treatment is with doxycycline. (A, B, D, G, H) *Borrelia*, *Ehrlichia*, *Francisella*, *Babesia*, and *Rickettsia* are all associated with ticks; however, they are less likely to be associated with hepatitis and endocarditis.

**39** A 54-year-old man presents to his physician complaining of difficulty with urination. He says that it requires increased efforts to urinate despite feeling the urge to void. He tells his physician that he would like to be screened for prostate cancer. He explains that his father was diagnosed with prostate cancer at age 68 and passed away at the age of 70 due to widespread metastatic disease. He wants to know if there is anything that can be done to see if he too has prostate cancer.

Which of the following is the most appropriate next action?

- (A) Order prostate serum antigen (PSA) levels
- (B) Explain that prostate cancer screening is not appropriate for him at this time
- (C) Discuss the advantages and disadvantages of screening
- (D) Reassure him that his risk of dying from prostate cancer is extremely low
- (E) Perform a digital rectal examination

**The answer is E: Perform a digital rectal examination.** This patient is presenting with difficulty voiding most likely secondary to benign prostatic hyperplasia (BPH). While his father's history is concerning for prostate cancer, BPH is a much more common cause of the symptoms he is describing. A full history and physical examination should first be performed, including a digital rectal examination to evaluate for signs of prostate enlargement. (A, B, C) At this time the American College of Physicians and American Cancer Society support informed decision making in deciding whether to perform PSA testing. PSA levels should not be ordered prior to a full discussion of the risks and benefits of screening with the patient. However, a digital rectal examination is the best answer for the next step in management since it addresses the likely cause of his chief complaint. (D) While it may be true that his risk of dying from prostate cancer is low, this is an uncertain and inappropriate comment at this time.

**40** A 65-year-old woman with a known history of Turner syndrome, GERD, and hypertension presents with acute onset of hemiparalysis of her right side. Her daughter explains that the symptoms began

while they were having lunch and her mother was having difficulty holding her utensils. She has no prior history of stroke or transient ischemic attacks. The daughter notes that her mother had surgery for a tooth abscess 1 month prior, and for the past 2 weeks has had intermittent fevers for which she took acetaminophen. Physical examination reveals a crescendo-decrescendo murmur best appreciated at the left upper sternal border and painful red lesions on her hands.

What could have prevented the development of the patient's current neurologic symptoms?

- (A) Maintaining good blood pressure control
- (B) IV antibiotic administration
- (C) Aortic valve replacement
- (D) Anticoagulation
- (E) Rapid plasma reagin testing

**The answer is B: IV antibiotic administration.** This woman presents with an acute stroke likely secondary to a septic embolus from infective endocarditis. Infective endocarditis occurs more commonly in individuals with predisposing valvular conditions such as a bicuspid aortic valve in Turner syndrome. Her dental procedure might have provided the source of infection; however, it is important to know that prophylactic antibiotics would not be recommended for a congenital bicuspid valve. In this case, treatment of the infective endocarditis with 4 to 6 weeks of IV antibiotic therapy based on culture specimens would have prevented her stroke.

(A) The cause of this patient's stroke was from a septic embolus, not vascular disease as a result of hypertension. (C) There is no history to suggest that she had an indication for valve replacement, and in addition prosthetic valves cause an increased risk of endocarditis. (D) While anticoagulation is indicated in those with mechanical heart valves or atrial fibrillation, this would not have prevented the endocarditis. (E) Rapid plasma reagin testing (RPR) is a screening test for syphilis. Though she has lesions on her palms, her history of a heart murmur and current stroke suggest that these lesions are most likely Osler nodes from infective endocarditis.

41

A 48-year-old man from Mexico presents for follow-up after recently being hospitalized for chest pain. The pain was pleuritic and relieved by leaning forward, and the cause was determined to be TB. He had no pulmonary symptoms, began treatment, and was discharged. Several months later, he complains of leg swelling and abdominal pain. His vital signs are within normal limits. He has jugular venous distention with pitting edema of the lower extremities. His lungs are clear to auscultation. He undergoes cardiac catheterization, and the pressure tracings are shown in *Figure 12-8*.

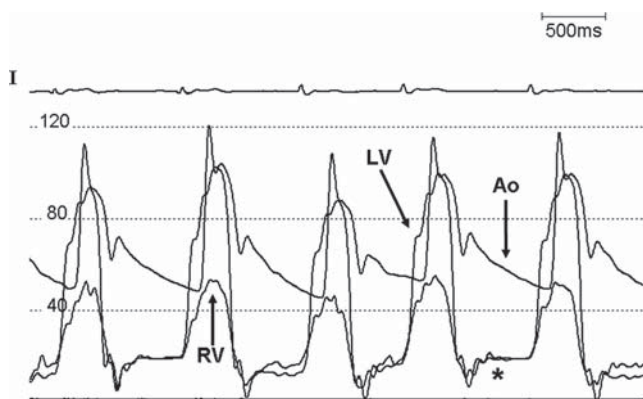


Figure 12-8

What is the correct diagnosis?

- (A) Reactivation tuberculosis
- (B) Medication effect
- (C) Pulmonary hypertension
- (D) Constrictive pericarditis

**The answer is D: Constrictive pericarditis.** This diagnosis should be considered in patients that previously experienced acute pericarditis (pleuritic chest pain relieved by leaning forward), especially when TB is the culprit. The findings of right heart failure (distended neck veins, leg swelling) without left heart failure (clear lungs) fits the diagnosis, although there may be some degree of left ventricular dysfunction (but not as severe as right ventricular dysfunction). The square-root sign (*asterisk* in figure) on cardiac catheterization is highly suggestive and is caused by a rapid increase in pressure at the onset of diastole with a subsequent plateau due to equalization of right ventricular and left ventricular end diastolic pressure. (A) This process is caused by adhesions of the two pericardial layers and fibrosis causing a rigid pericardium, not by reactivation of TB. (B) The anti-TB medications have important toxicities, but they do not cause right heart failure. (C) Pulmonary hypertension can cause right heart failure; however, there is no historical clues that explain why this patient would have this diagnosis; the recent diagnosis of TB pericarditis makes constrictive pericarditis much more likely.

42

A 70-year-old woman presents with complaints of a change in her voice. She first noticed hoarseness several weeks ago, which has progressively worsened. She has a longstanding history of Hashimoto thyroiditis, for which she takes levothyroxine. She is otherwise healthy. Physical examination reveals a diffusely enlarged thyroid.

What is the next appropriate step in management?

- (A) Increase levothyroxine dose
- (B) Check serum TSH level
- (C) Decrease levothyroxine dose
- (D) Fine needle aspiration biopsy
- (E) Radioactive iodine uptake scan

**The answer is D: Fine needle aspiration biopsy.** Patients with a long-standing history of Hashimoto thyroiditis are at a 60×-increased risk of lymphoma of the thyroid, which is most often non-Hodgkin lymphoma. Although thyroid lymphoma is rare (1% to 2% of thyroid malignancies), the association with longstanding Hashimoto thyroiditis is significant. Patients often present with the symptoms of a rapidly enlarging neck mass. A fine needle aspiration biopsy will confirm the diagnosis, along with differentiating the mass from other types of thyroid cancer. (A, B, C, E) The absence of other symptoms decreases the likelihood of an endocrine process, and it is important to rule out cancer given the patient's history of Hashimoto thyroiditis.

43

A previously healthy 64-year-old woman presents with bright red blood per rectum and dizziness. She reports that the bleeding started approximately 7 hours ago and has never occurred before. The bleeding is painless. Laboratory values reveal a hemoglobin of 7.9 g/dL.

Which of the following is the most likely diagnosis?

- (A) Diverticulitis
- (B) Diverticulosis
- (C) Colon cancer
- (D) Inflammatory bowel disease

**The answer is B: Diverticulosis.** This patient is presenting with a massive lower GI bleed, which is indicated by *bright* red blood per rectum, as opposed to melena, which is pitch-black stool indicative of an upper GI bleed. The most common cause of massive and painless bright red blood per rectum is diverticulosis. Other causes include angiodysplasia, which may be associated with aortic stenosis (a result of shearing of von Willebrand factor). Diverticulosis is treated with a diet rich in fiber. (A) Diverticulitis presents with abdominal pain and fever and does not typically have significant rectal bleeding. (C) Colon cancer is a common cause of lower GI bleeding, but there are no other clues that this is the diagnosis (no previous symptoms of stool changes, weight loss, abdominal pain, etc.). (D) It would be unusual for inflammatory bowel disease to present at this age.

44

A 55-year-old man with a 50 pack-year smoking history presents to the Emergency Department with complaints of subjective fever, cough, dyspnea, and right-sided pleuritic chest pain. The symptoms began

1 week ago and have worsened over the last 4 days. On physical examination, he has decreased breath sounds, dullness to percussion, egophony, and decreased tactile fremitus over the right lung base. An upright chest x-ray reveals a consolidation in the right lower lobe and a pleural effusion with 2 cm of fluid; the right lateral decubitus view shows evidence of loculation. A thoracentesis is performed and the pleural fluid is analyzed. Empiric antibiotics are started. Gram stain of the fluid, culture of the fluid, and two sets of blood cultures are pending.

Which of the following pleural fluid analyses are most consistent with this patient's diagnosis?

- (A) Leukocyte count of 5,000/mm<sup>3</sup> (80% neutrophils, 18% lymphocytes, 2% macrophages), pH 6.98, LDH 2,000 U/L, glucose 40 mg/dL
- (B) Leukocyte count of 3,500/mm<sup>3</sup> (20% neutrophils, 60% lymphocytes, 10% macrophages, 5% mesothelial cells, 6% eosinophils), pH 7.35, LDH 240 U/L, glucose 68 mg/dL
- (C) Leukocyte count of 800/mm<sup>3</sup> (20% neutrophils, 65% lymphocytes, 10% mesothelial cells, 4% eosinophils), pH 7.5, LDH 250 U/L, glucose 70 mg/dL, triglycerides 145 mg/dL
- (D) Leukocyte count of 500/mm<sup>3</sup> (30% neutrophils, 65% lymphocytes, 2% mesothelial cells, 3% eosinophils) pH 7.45, LDH 100 U/L, glucose 80 mg/dL

**The answer is A: Leukocyte count of 5,000/mm<sup>3</sup> (80% neutrophils, 18% lymphocytes, 2% macrophages), pH 6.98, LDH 2,000 U/L, glucose 40 mg/dL.** This patient has symptoms (fever, cough, dyspnea, and pleuritic chest pain) and signs (decreased breath sounds, dullness to percussion, and egophony) that are consistent with community-acquired pneumonia. Decreased tactile fremitus supports the radiographic findings of parapneumonic effusion complicating the pneumonia. Parapneumonic effusions resulting from infection such as pneumonia are typically exudative. An LDH value >two-thirds the upper limit of normal is one of the Light criteria. (B) A tuberculous exudative effusion would have a lymphocyte predominance. (C) Elevated triglycerides in the pleural effusion is consistent with a chylothorax. (D) Transudative effusions are commonly seen with congestive heart failure, nephrotic syndrome, or cirrhosis.



45 A 60-year-old man with a history of diabetes mellitus, hypertension, and hyperlipidemia presents to the primary care clinic with complaints of bilateral hand tremor which began 4 years ago but has been worse in the last year. He states that the tremor gets worse when he tries to eat or write. He notes that both his mother and his brother had a similar tremor. He does not drink alcohol, he smokes 1 pack of cigarettes daily, and he denies any recreational drug use. His medications include

metformin, lisinopril, and atorvastatin. On examination he has a mild tremor in both upper extremities that is evoked when he holds his arms outstretched. There is no tremor while the patient is sitting at rest. There is no vocal tremor. Gait examination is normal.

What is the best treatment for this patient's tremor?

- (A) Propranolol
- (B) Carbidopa–levodopa
- (C) Donepezil
- (D) Phenobarbital
- (E) Memantine

**The answer is A: Propranolol.** This patient has essential tremor as evidenced by its exacerbation with intention (worse with writing and eating) and when maintaining a posture on examination. Essential tremor usually has an autosomal dominant inheritance, supported by a family history of the same tremor in the patient's mother and brother. Propranolol is the first-line treatment. (B) Carbidopa–levodopa is a treatment for Parkinson disease, which features a resting, but not intentional tremor. (C) Donepezil is a central-acting acetylcholinesterase inhibitor used in the treatment of Alzheimer disease. (D) Phenobarbital is a barbiturate and has had conflicting outcomes for essential tremor, thus it is not first line. (E) Memantine is an NMDA receptor antagonist used in the treatment of Alzheimer disease.

46

A 56-year-old man develops acute swelling of his left lower leg. He says that he was at work when he first noticed that his leg felt swollen. He has had multiple previous episodes of swelling in both his left and right legs over the past year. An ultrasound is performed and reveals a superficial vein thrombosis of his lower calf. He is started on anticoagulation.

Which of the following tests would most likely be elevated in this patient?

- (A) CA-125
- (B)  $\alpha$ -fetoprotein (AFP)
- (C)  $\beta$ -hCG
- (D) CA 19–9
- (E) CEA
- (F) Calcitonin
- (G) PSA

**The answer is D: CA 19–9.** This patient has signs of recurrent superficial thrombophlebitis, a condition that is associated with underlying malignancies (specifically, adenocarcinomas of the pancreas and lung). CA 19–9 is a marker that may be elevated in cancers of the pancreas, bile duct, gall bladder, or stomach. While it is most useful in the assessment of response to treatment, it can be expected to be elevated in individuals with pancreatic cancer.

(A) CA-125 is a tumor marker specific for ovarian cancer that may be used in diagnosis and assessment of treatment response. (B)  $\alpha$ -fetoprotein may be elevated in liver cancers and germ cell tumors. It is useful in the diagnosis of hepatocellular carcinoma and the staging of germ cell tumors. (C)  $\beta$ -hCG is a marker of choriocarcinoma and testicular cancer. It is most useful in the staging of cancers and may be prognostic for individual response to treatment. (E) CEA is a marker of colorectal and breast cancers. It can be used to assess colorectal cancer spread and breast cancer recurrence. (F) Calcitonin is elevated in medullary thyroid cancer and may be used in diagnosis. It may be monitored to assess efficacy of treatment or to identify recurrence. (G) PSA is often elevated in prostate cancer. It may be useful in diagnosis, determining individual response to treatment, and identifying recurrence of disease.

47

A 52-year-old woman presents with severe abdominal pain for the last 8 hours. She describes the pain as sharp and localized to her upper abdomen. The pain radiates to her back and she has vomited three times. The patient notes that she has been hospitalized several times in the past with similar complaints. She has a blood pressure of 140/80 mmHg, pulse of 108/min, temperature of 36.6°C, and respiratory rate of 18 breaths per minute. Physical examination demonstrates tenderness to palpation in the epigastric area.

Which of the following is the next step in the diagnosis of this patient's condition?

- (A) Abdominal CT scan
- (B) Serum lipase and liver function tests
- (C) Abdominal ultrasound
- (D) Proceed to treatment, no further work-up necessary

**The answer is B: Serum lipase and liver function tests.** This patient is presenting with signs and symptoms consistent with acute pancreatitis (upper abdominal pain radiating to the back). Given that these symptoms are non-specific and could indicate other abdominal pathology, diagnosis must be confirmed with serum amylase and lipase (more specific) levels. Liver function tests, including an alkaline phosphatase level, should be ordered as well to determine if there are gallstones or common bile duct obstruction (a cause of pancreatitis).

48

A 36-year-old man presents to the hospital with fever and leg swelling. His right lower extremity has a large area of erythema and swelling, and there is purulent drainage from a small area on the leg. He is admitted to the hospital and begins treatment with IV antibiotics. He suddenly develops flushing and pruritus of his face, chest, and upper extremities.



What should be done next?

- (A) Stop the antibiotic immediately
- (B) Add an additional antibiotic to his empiric regimen
- (C) Immediate surgical debridement
- (D) Slow down the infusion rate of the antibiotic
- (E) Administer intramuscular epinephrine

**The answer is D: Slow down the infusion rate of the antibiotic.** This patient has cellulitis concerning for MRSA given the purulent drainage. Vancomycin is an appropriate treatment, and a well-known side effect of rapid vancomycin administration is red man syndrome, which is represented by the findings seen in this patient. The rate of administration should be slowed down and the antibiotic should be given over 60 minutes. (A, B) The vancomycin does not need to be stopped, and this sudden presentation is too fast for the infection to spread, so adding an additional antibiotic is not worthwhile. (C) Surgical debridement is necessary for necrotizing fasciitis, which would have signs of necrosis and crepitus on examination. (E) Severe red man syndrome may mimic anaphylaxis, but it would present with vital sign changes and angioedema (which are not mentioned in the vignette).

49

A 37-year-old woman is brought in to the psychiatric Emergency Department after being found running partially clothed down a major roadway. Vitals on intake reveal a temperature of 39.8°C, a blood pressure of 158/61 mmHg, a heart rate of 144 beats per minute, and a respiratory rate of 23 breaths per minute. The patient vomits after vitals are collected. The psychiatry attending immediately orders a thyroid function test and sends the patient to the medical emergency room.

After arrival in the ER, what is the best next step in management?

- (A) Give oral methimazole
- (B) Give oral iodine to block release of thyroid hormones from the thyroid gland
- (C) Immediate transport to the operating room for thyroidectomy
- (D) Administer propranolol, propylthiouracil (PTU), and hydrocortisone
- (E) Give IV hydrocortisone to counteract limited adrenal reserve

**The answer is D: Administer propranolol, propylthiouracil (PTU), and hydrocortisone.** This patient is exhibiting symptoms of thyroid storm, which is a life-threatening disorder that requires immediate control of heart rate (with a  $\beta$ -blocker), inhibition of thyroid hormone synthesis (with a thionamide), and reduction of T4 to T3 conversion (with a glucocorticoid). (A, E) Methimazole or corticosteroids are insufficient treatments of thyroid storm, as  $\beta$ -blockers are needed to control the patient's tachycardia.

(B) Iodine is used acutely in the treatment of thyroid storm but is given 1 hour after thionamide administration. (C) Thyroidectomy can be used in patients unable to receive thionamides; however,  $\beta$ -blockers and glucocorticoids must be given first.

50

A 23-year-old woman presents to her primary care physician complaining of fever and pain in her wrists and fingers. She has also noted several painless “bumps” on her skin. She is sexually active with multiple partners and her last menstrual period ended 5 days ago. She does not endorse any vaginal pain or discharge. Physical examination reveals bilateral tenderness of her wrists and several interphalangeal joints as well as several lesions on her hands and forearms (*Figure 12-9*). Ocular examination is benign.



Figure 12-9

Which of the following is the next best step in management?

- (A) Two sets of blood cultures
- (B)  $\beta$ -hCG urine test
- (C) Synovial fluid culture
- (D) Aspartate transaminase (AST) and alanine transaminase (ALT)
- (E) Empiric ceftriaxone

**The answer is A: Two sets of blood cultures.** The patient most likely has disseminated gonococcal disease. (E) However, *Neisseria meningitidis* and *Staphylococcus aureus* can mimic this presentation and should be excluded by blood culture prior to administration of antibiotics. Disseminated gonococcus typically presents as either a triad of dermatitis (hemorrhagic vesiculopustular lesions), tenosynovitis, and arthralgia without arthritis or purulent arthritis without skin lesions. (C) This patient has the former presentation; therefore a synovial fluid culture would be low yield. (B) Pregnancy is a risk factor for disseminated gonorrhea and should be excluded in all patients

without recent menstruation (this patient's menstrual period ended 5 days ago). (D) Hepatitis B, which causes hepatocellular damage, can present with polyarthrititis and tenosynovitis but is more likely to be associated with an urticarial rash.

51

A 45-year-old man with a history of chronic hepatitis C infection presents with severe upper gastrointestinal bleeding. Intravenous fluids and packed red blood cells are administered; however, the patient becomes oliguric. Laboratory values reveal a BUN of 62 mg/dL and a creatinine of 4.2 mg/dL. His BUN and creatinine values at a previous appointment 3 months ago were 21 mg/dL and 1.8 mg/dL, respectively.

Which of the following is the definitive treatment of choice for this patient's condition?

- (A) Pegylated interferon- $\alpha$  and ribavirin
- (B) Liver transplantation
- (C) Midodrine
- (D) Albumin
- (E) Intravenous normal saline

**The answer is B: Liver transplantation.** This patient is presenting with hepatorenal syndrome, a life-threatening medical condition that involves rapid deterioration in kidney function in patients with cirrhosis. (C, D) Although renal function can sometimes be improved by administration of albumin and systemic vasoconstrictors (midodrine), hepatorenal syndrome is usually fatal unless a liver transplantation is performed. (A) This is the treatment of hepatitis C; however, this patient has progressed to irreversible end stage liver disease. (E) If the patient had prerenal AKI, he might respond to IV fluids; however, he had an elevated creatinine at a previous appointment and therefore likely has chronic renal failure from hepatorenal syndrome.

52

A 36-year-old woman presents to the clinic with fever and cough. A thorough history is taken, which is notable for night sweats and weight loss over the past 3 months. She was born in Mexico and moved to the United States when she was 31 years old. She denies using any tobacco, alcohol, or illicit drugs. Her laboratory values are notable for a hemoglobin of 10.1 g/dL, and a chest x-ray shows a right upper lobe infiltrate with cavitation.

What is the most important treatment at this time?

- (A) Voriconazole
- (B) Isoniazid and pyridoxine
- (C) Rifampin, isoniazid, pyrazinamide, and ethambutol
- (D) Rifampin, isoniazid, pyrazinamide, pyridoxine, and ethambutol
- (E) Levofloxacin

**The answer is D: Rifampin, isoniazid, pyrazinamide, pyridoxine, and ethambutol.** This patient's symptoms, as well as her risk factor (immigration from an endemic country), make TB a concerning diagnosis. Though an AFB smear and culture should be performed to confirm the diagnosis, she should begin a four-drug therapy for 2 months followed by a two-drug therapy (rifampin and isoniazid) for 4 months. (C) Pyridoxine (vitamin B<sub>6</sub>) should be given to prevent peripheral neuropathy from isoniazid. (B) Treatment with isoniazid and pyridoxine alone is an option for the treatment of latent TB, as opposed to active TB, which is the diagnosis in this case. (A) Voriconazole is a treatment option for *Aspergillus* (not fluconazole, which does not have activity against *Aspergillus*); however, TB is the more likely diagnosis in this case given her risk factors. (E) Levofloxacin can be used as empiric treatment for community-acquired pneumonia.

53

A 39-year-old man falls off a sailboat and is found much later floating face down in a lake. He is pulled from the water and efforts are made to resuscitate him. A pulse is regained in the ambulance, but he experiences a seizure during transport to the hospital.

What electrolyte abnormality is most likely responsible for this occurrence?

- (A) Hyperkalemia
- (B) Hypernatremia
- (C) Hypercalcemia
- (D) Hypokalemia
- (E) Hyponatremia
- (F) Hypocalcemia

**The answer is A: Hyperkalemia.** Prolonged water immersion can induce hypothermia in patients, which can lead to rhabdomyolysis and subsequent release of large amounts of potassium from muscle cells. Prolonged vasoconstriction from shivering and hypoxia may also contribute. (D) Hypokalemia is not associated with seizures and is most commonly due to gastrointestinal or renal losses. (B, E) While both hypernatremia and hyponatremia may cause neurologic symptoms such as seizures, they are not associated with hypothermia. (C, F) Hypercalcemia is associated with nephrolithiasis, abdominal pain, bone wasting, and psychiatric symptoms, but does not commonly cause seizures; hypocalcemia may present with paresthesia.

54

A 22-year-old woman presents to the office complaining of episodes where her fingers become painful and change color. Her fingers first become cold and pale, then turn blue, and after warming them her fingers become red. She brings in a picture to illustrate what it looks like (*Figure 12-10*).



**Figure 12-10**

She states that this commonly occurs when she shops in the frozen section at a supermarket. She has tried to wear gloves to keep her hands warm but this has not reduced the occurrences of her symptoms. She denies any numbness or weakness of her arms or legs. On examination she has several small ulcerations at the tips of her fingers, with strong pulses present.

What is the best treatment for this patient?

- (A) Corticosteroids
- (B) Nifedipine
- (C) Sildenafil
- (D) Prazosin
- (E) No treatment is necessary at this time

**The answer is B: Nifedipine.** This patient presents with Raynaud phenomenon, which follows the chronologic color pattern of white to blue to red during episodes. Initial treatment includes avoidance of triggers and measures to maintain warmth of the affected areas, but this patient has failed these treatments. The first-line pharmacologic therapy is the dihydropyridine calcium channel blockers such as nifedipine. (C, D) Sildenafil or prazosin may be considered in patients who are intolerant of calcium-channel blockers. (A) Corticosteroids are used in the treatment of many autoimmune conditions that are associated with Raynaud phenomenon, but should not be used solely to treat Raynaud phenomenon. (E) Without treatment, ischemic episodes may progress to necrosis requiring amputation of a digit.

55

A 36-year-old man comes to the office for a routine visit. He has not seen a doctor in over 15 years, but his wife insisted he go for a “checkup.” He has no medical problems or complaints. He has smoked half a pack of cigarettes for the last 10 years. His vitals show a temperature of 37.2°C, blood pressure of 148/82 mmHg, heart rate of 70 beats per minute, and respiratory rate of 12 breaths per minute. His BMI is 28 kg/m<sup>2</sup>. Repeat

blood pressure measurement shows 152/88 mmHg. His physical examination is unremarkable. His laboratory values are shown below.

|                      |                       |
|----------------------|-----------------------|
| Hemoglobin           | 14.5 g/dL             |
| Leukocyte count      | 7,500/mm <sup>3</sup> |
| Sodium               | 139 mEq/L             |
| Potassium            | 4.1 mEq/L             |
| Creatinine           | 0.9 mg/dL             |
| Random blood glucose | 98 mg/dL              |

He is counseled on maintaining a healthy diet, exercise, and smoking cessation.

What is the best next step in management?

- (A) Initiate hydrochlorothiazide
- (B) Initiate lisinopril
- (C) Obtain an ECG
- (D) Recheck blood pressure in 2 weeks
- (E) Routine follow-up

**The answer is D: Recheck blood pressure in 2 weeks.** Hypertension cannot be diagnosed in a single office visit, as the diagnosis of hypertension should be confirmed on three separate visits prior to the initiation of pharmacologic therapy unless the blood pressure elevation is moderate to severe. The best answer is to have the patient return in 2 weeks, at which time his blood pressure can be checked again. Given his age, he should also have a lipid panel performed. (A, B) It is inappropriate to initiate medication before the diagnosis is confirmed. (C) An ECG is not recommended at this time. (E) The patient has an elevated blood pressure, and if left untreated, may produce eventual end-organ damage.



A 20-year-old college student presents to the urgent care office complaining of a sore throat, mild cough, and runny nose for the past 2 days. The patient is diagnosed with an upper respiratory tract infection and he is offered symptomatic treatments. As he is leaving the office, he complains of a several-day history of exquisite penile tenderness that has since resolved. He denies any other associated symptoms but does endorse sexual activity with occasional condom use. Genitourinary examination demonstrates a normal penile shaft without

evidence of lesions, erythema, or discharge from the meatus. There is mildly tender inguinal lymphadenopathy.

What is the most likely etiology?

- (A) Human papillomavirus (HPV)
- (B) *Neisseria gonorrhoeae*
- (C) Human immunodeficiency virus (HIV)
- (D) *Treponema pallidum*
- (E) Herpes Simplex Virus, type 2 (HSV-2)
- (F) *Trichomonas vaginalis*
- (G) *Haemophilus ducreyi*
- (H) *Escherichia coli*
- (I) *Chlamydia trachomatis*
- (J) Conversion disorder

**The answer is E: Herpes Simplex Virus, type 2.** A history of painful genitalia in an adolescent or young adult with a normal genitourinary physical examination is most suggestive of genital herpes infection. Classically, HSV-2 infection presents with multiple painful fluid-filled vesicles with an erythematous base that eventually burst and crust over; however, many patients do not present until the ulcers have fully healed and many patients may not notice the lesions themselves. By the time patients present to a physician, the physical examination may be benign. (A) HPV presents with multiple nonpainful verrucous lesions. (B, D, I) These infections often present with urethral discharge. (C) This patient is at risk for HIV, but does not have any symptoms of acute retroviral syndrome. (F) *Trichomonas* presents in women with vaginal discharge. (G) Evidence of tender inguinal lymphadenopathy is found in chancroid (*Haemophilus ducreyi*), but this infection is exceedingly rare in the United States and mildly tender lymphadenopathy is not an unusual finding in patients with genital herpes. (H) *E. coli* causes UTIs and is not an STI. (J) Always rule out medical conditions before making psychiatric diagnoses.

57

A 24-year-old woman is brought in by ambulance to the Emergency Department following a motor vehicle accident. She is complaining of right flank and abdominal pain. Physical examination is notable for a large ecchymosis over the right flank. A urinalysis is remarkable for 38 RBCs per high-power field.

What is the most likely site of injury?

- (A) Kidney
- (B) Ureter
- (C) Bladder
- (D) Liver
- (E) Urethra

**The answer is A: Kidney.** Hematuria on urinalysis localizes the injury to the genitourinary tract, and this patient likely has a renal hematoma given the right flank pain and ecchymosis on physical examination. **(B, C)** Ureters are highly protected during trauma, and a bladder injury would present with suprapubic pain and peritoneal signs. **(D)** Liver injuries do not present with hematuria. **(E)** If this were a male, a urethral tear would also be possible from rapid deceleration.

**58** A 49-year-old woman with a history of colorectal cancer is brought to the Emergency Department with chest pain. She is found to be tachycardic and tachypneic. An ECG is normal. Upon questioning, she states that she remains in bed all day. CT angiography reveals that she has a pulmonary embolism. She is started on low-molecular-weight heparin and is admitted. Three days later, her laboratory values are drawn.

|                 |                        |
|-----------------|------------------------|
| Hemoglobin      | 13.4 g/dL              |
| Leukocyte count | 9,500/mm <sup>3</sup>  |
| Platelets       | 60,000/mm <sup>3</sup> |

On admission, her platelet count was 180,000/mm<sup>3</sup>. A serotonin release assay is sent and returns positive.

What is the best next step in management?

- (A)** Transfuse platelets
- (B)** Switch to IV heparin
- (C)** Switch to IV argatroban
- (D)** Switch to clopidogrel and aspirin
- (E)** Continue the low-molecular-weight heparin

**The answer is C: Switch to IV argatroban.** This patient likely has heparin-induced thrombocytopenia, which is an immune-mediated response to unfractionated or low-molecular-weight heparin. The best option is to discontinue the low-molecular-weight heparin and switch to an alternative anticoagulant such as argatroban. **(A)** A platelet count of 60,000/mm<sup>3</sup> is not an indication for transfusion. **(B)** The risk of heparin-induced thrombocytopenia is much lower with low-molecular-weight heparin than unfractionated heparin, so switching to unfractionated heparin is a poor choice. **(D)** Clopidogrel and aspirin are antiplatelet medications and are not appropriate for treating a pulmonary embolism. **(E)** When this complication is recognized, the heparin product should be discontinued immediately.

**59** An 80-year-old woman with a history of atrial fibrillation, dementia, and frequent falls is admitted to the hospital for a UTI. She has no history of stroke. The family is at the bedside and is requesting clarification on her medication requirements, as they are her primary caregivers.



What is the proper anticoagulation regimen for this patient?

- (A) Stop all anticoagulation until the UTI resolves
- (B) Aspirin only
- (C) Warfarin only
- (D) Aspirin and warfarin
- (E) Aspirin and heparin

**The answer is B: Aspirin only.** It is important to be familiar with the CHADS<sub>2</sub> scoring system for anticoagulation in atrial fibrillation. An 80-year-old with a-fib and no other risk factors would have a score of 1, which may be treated with warfarin or aspirin. (C, D) Aspirin alone is the better option since her frequent falls give her an increased risk of bleeding. (A) It is important to continue anticoagulation unless the patient is actively bleeding. (E) Heparin is used as an anticoagulant bridge until the effect of warfarin becomes therapeutic.

60

A 36-year-old man presents with a severe headache that began a few hours ago. He has no prior history of headaches but does have a prior history of “kidney cysts.” His wife meets him in the Emergency Department and says that his uncle experienced something similar to this a few years ago. A CT scan shows signs of subarachnoid hemorrhage. Further imaging reveals a berry aneurysm. Neurosurgery performs an endovascular coiling procedure and the patient returns home a few days later. One week after discharge, the patient’s wife brings him back because of increased sleepiness and confusion. On examination, his temperature is 37°C, blood pressure is 135/86 mmHg, pulse is 85/min, and respiratory rate is 14 breaths per minute. His neurologic examination is normal, and his laboratory values are shown below.

|                     |                         |
|---------------------|-------------------------|
| Hemoglobin          | 13.9 g/dL               |
| Leukocyte count     | 8,900/mm <sup>3</sup>   |
| Platelets           | 300,000/mm <sup>3</sup> |
| Sodium              | 121 mEq/L               |
| Potassium           | 4.6 mEq/L               |
| Blood urea nitrogen | 15 mg/dL                |
| Creatinine          | 0.8 mg/dL               |
| Glucose             | 96 mg/dL                |

What is the most likely explanation for this patient's current state?

- (A) Recurrent bleeding
- (B) Psychogenic polydipsia
- (C) Meningitis
- (D) Brain stem herniation
- (E) Cerebral salt-wasting

**The answer is E: Cerebral salt-wasting.** This patient is presenting with symptomatic hyponatremia after a recent neurosurgical procedure for management of a subarachnoid hemorrhage. Cerebral salt-wasting is associated with subarachnoid hemorrhage and classically presents a few days after neurosurgical procedures. While the exact mechanism is unclear, it may be similar to the syndrome of inappropriate ADH (SIADH) in that it leads to a net loss of sodium in the urine.

(A) While recurrent bleeding is a possibility in this patient, this would present with symptoms similar to his first episode and would likely be more rapid in onset. (B) This patient has no history of psychiatric disorders, thus psychogenic polydipsia is an unlikely diagnosis. (C) Meningitis would not fully explain the patient's profound hyponatremia. In addition, he is afebrile without leukocytosis. (D) Brain stem herniation may lead to dysregulation of breathing and other autonomic processes and often progresses to death. This has a much more rapid onset and progression in addition to neurologic signs on examination.

61

A 45-year-old woman with no significant medical history presents to the clinic with progressive shortness of breath, dry cough, subjective fever, and chills for the last 4 weeks. Three weeks ago, she presented to the Emergency Department with the same complaints and a chest radiograph at that time revealed minimal consolidation in the left lower lobe. She was given a course of azithromycin, which failed to improve her symptoms. She has never smoked, usually runs 3 miles daily, and has been working as a secretary for the last 20 years. She has not traveled recently and has no sick contacts. On examination, her temperature is 37.6°C, blood pressure is 120/80 mmHg, and heart rate is 75 beats per minute. Cardiac examination is normal. Lung examination reveals scattered rales. Chest radiograph today reveals a consolidation in the right middle lobe.

What is the most likely diagnosis?

- (A) Community-acquired pneumonia
- (B) Idiopathic pulmonary fibrosis
- (C) Silicosis
- (D) Berylliosis
- (E) Cryptogenic organizing pneumonia

**The answer is E: Cryptogenic organizing pneumonia.** Cryptogenic organizing pneumonia (COP), also known as bronchiolitis obliterans organizing pneumonia (BOOP), often presents with subacute development of non-specific constitutional symptoms including weight loss, fever, chills, and night sweats. Dyspnea and dry cough are also important historical features. **(A)** This subacute and progressive development of symptoms differentiates COP from CAP, which is often acute in presentation. Patients with COP have often been diagnosed with CAP in the past but fail to respond to treatment. Radiographic findings reveal “migrating” alveolar processes. **(C, D)** This patient has no exposure history to support silicosis or berylliosis as the diagnosis. **(B)** Idiopathic pulmonary fibrosis (IPF) typically presents with a more prolonged course than COP and radiographic findings show a reticulonodular/interstitial process.

62

A 68-year-old man with a history of hypertension and diabetes presents with fatigue and a 4.5-kg (10-lb) weight loss over the past 6 months. He denies hematochezia, melena, diarrhea, nausea, and vomiting. Laboratory findings reveal a hemoglobin level of 10.1 g/dL. Fecal occult blood test (FOBT) is positive.

Which of the following is the best next step in the management of this patient?

- (A)** Abdominal and pelvic CT scan
- (B)** Sigmoidoscopy
- (C)** Colonoscopy
- (D)** Reassurance

**The answer is C: Colonoscopy.** This patient is presenting with anemia (likely secondary to iron deficiency) and positive FOBT. Any older patient presenting with iron-deficiency anemia and positive FOBT must be evaluated with colonoscopy to determine if the underlying etiology is malignancy (colon cancer).

63

A 55-year-old woman presents to her primary care doctor complaining of shortness of breath, cough, and swelling of her face and right arm. Her medical history is significant for COPD, hypertension, and diabetes. She has an 80 pack-year smoking history. Physical examination reveals superficial venous engorgement over her chest with a plethoric face. Her right pupil is smaller than her left.

What is the most likely diagnosis?

- (A)** Pulmonary embolism
- (B)** Pancreatic cancer
- (C)** COPD exacerbation
- (D)** Bronchogenic carcinoma
- (E)** Ischemic stroke

**The answer is D: Bronchogenic carcinoma.** This patient has dyspnea, venous congestion in her face and arm, and Horner syndrome, which can all be explained by compression of nearby structures by lung cancer. This is called superior vena cava (SVC) syndrome, and is most often caused by bronchogenic carcinoma. (A) Pulmonary embolism would present with dyspnea, tachycardia, and positive risk factors for clotting (e.g., presence of a DVT). (B) Pancreatic cancer and other GI malignancies are associated with migratory thrombophlebitis; however, the rest of the symptoms/signs suggest SVC syndrome. (C) A COPD exacerbation would not present with superficial venous engorgement. (D) Anisocoria (difference in size between pupils) can be caused by any disruption in sympathetic or parasympathetic innervation to the pupil. A stroke would not fit the rest of this patient's findings.

64

A 53-year-old woman with a history of nonischemic cardiomyopathy and paroxysmal atrial fibrillation presents to the Emergency Department with worsening shortness of breath for the last 3 days. She has also noticed increased swelling in her legs and decreased exercise tolerance. She used to do her grocery shopping for herself but now becomes too fatigued going to the grocery store and has her son do her shopping instead. She also reports intermittent diarrhea, palpitations, and sweating at night. Her laboratory values are shown below.

|                           |                                     |
|---------------------------|-------------------------------------|
| Hemoglobin                | 9.0 g/dL                            |
| Leukocyte count           | 6,400/mm <sup>3</sup>               |
| Brain natriuretic peptide | 906 pg/mL (normal range ≤100 pg/mL) |
| TSH                       | 0.1 μU/mL                           |
| Free T4                   | 43 μg/dL                            |

Which of her medications should be stopped?

- (A) Carvedilol
- (B) Lisinopril
- (C) Iron sulfate
- (D) Amiodarone
- (E) Warfarin

**The answer is D: Amiodarone.** The patient described above is having an exacerbation of her heart failure, as evidenced by her worsening shortness of breath and leg swelling. One possible cause of this CHF exacerbation is hyperthyroidism, which is supported by her symptoms of diarrhea,

palpitations, and night sweats, as well as her low TSH and elevated free T4 laboratory values. Of the listed medications, amiodarone is the only one that has the possibility of causing hyperthyroidism and should be discontinued. Amiodarone can also cause pulmonary fibrosis leading to shortness of breath.

65

A 24-year-old man presents for evaluation of a rash. Over the last 3 months, the rash has progressed from his scalp and face to his upper shoulders and back. The patient also endorses dandruff that has persisted even with the use of over-the-counter dandruff shampoo. The patient endorses pruritus but has no other complaints. Physical examination reveals erythematous plaques with greasy scale (Figure 12-11).



Figure 12-11

Which of the following is the best next step in management of this patient?

- (A) Skin biopsy
- (B) HIV testing
- (C) Fungal cultures
- (D) Ketoconazole treatment

**The answer is B: HIV testing.** This patient is presenting with the classic signs of seborrheic dermatitis. Erythematous plaques with greasy scale and indistinct margins describe seborrheic dermatitis. Seborrheic dermatitis is very common in HIV infection and can actually be the presenting feature. Up

to 80% of HIV/AIDS patients have seborrheic dermatitis and these patients present with a greater severity. New onset of severe seborrheic dermatitis should prompt the practitioner to consider HIV infection.

**66** A 24-year-old woman presents to her primary care physician complaining of headache, fever, and pain and itching in her genital region. She is currently sexually active and uses condoms “sometimes.” On examination, her vital signs are: temperature of 37.9°C, blood pressure of 117/74 mmHg, heart rate of 87 beats per minute, and respiratory rate of 16 breaths per minute. Physical examination was significant for several tender, ulcerating, pustular lesions on his genitals and tender inguinal lymphadenopathy.

Which of the following tests could diagnose the cause of her symptoms?

- (A) Dark field microscopy
- (B) Tzanck smear
- (C) Pathergy reaction test
- (D) Gram stain
- (E) Tissue crush preparation and staining

**The answer is B: Tzanck smear.** The patient is experiencing a primary herpes infection. (A) Dark field microscopy is used to diagnose syphilis, which would typically present with a solitary *painless* genital ulcer. (C) Behçet disease, diagnosed by a pathergy reaction test, would typically present with oral and cutaneous ulcers and is not associated with lymphadenopathy. (D) Chancroid, which would be diagnosed with a gram stain, could also present as multiple painful ulcers and inguinal lymphadenopathy, but is unlikely to cause systemic symptoms. (E) Donovanosis (*granuloma inguinale*) is caused by *Klebsiella granulomatis* and causes *painless* ulcers. It is diagnosed by tissue crush preparation.

**67** A 68-year-old man presents with a cough for the last 6 months. He noticed 2 days ago that the cough also had thin streaks of bright red blood. He denies any fever, chills, or weight loss. He smokes 1 pack of cigarettes per day for the last 40 years. Vital signs are within normal limits and lung examination reveals decreased breath sounds diffusely. Chest x-ray does not show any abnormalities.

What is the best next step for this patient?

- (A) Bronchoscopy
- (B) CT scan of the chest
- (C) Begin empiric antibiotics
- (D) Repeat chest x-ray in 3 months

**The answer is B: CT scan of the chest.** The differential diagnosis of hemoptysis in a smoker includes bronchitis, malignancy, pneumonia, and mechanical trauma from excessive coughing. **(D)** Given his risk for malignancy, he should be further evaluated with a CT scan of the chest rather than repeating a chest x-ray in 3 months. **(A)** If a mass adjacent to the airway is found, it can be further evaluated with bronchoscopy. **(C)** This patient does not have a fever, chills, or x-ray findings suggestive of pneumonia, thus empiric antibiotics would not be appropriate at this time.

68

A 65-year-old woman with a past medical history of congestive heart failure presents with increasing confusion. The patient is unable to respond to questions in a coherent manner. Her son says that she has been drinking a pint of brandy a day for the past 40 years and expresses concern that her drinking has increased in the past few months since his father passed away. A chest x-ray shows an enlarged heart but is otherwise normal. Her laboratory values are shown below.

|                     |                         |
|---------------------|-------------------------|
| Hemoglobin          | 11.5 g/dL               |
| Leukocyte count     | 8,000/mm <sup>3</sup>   |
| Platelets           | 180,000/mm <sup>3</sup> |
| Sodium              | 141 mEq/L               |
| Potassium           | 4.0 mEq/L               |
| Blood urea nitrogen | 45 mg/dL                |
| Creatinine          | 2.5 mg/dL               |
| Glucose             | 105 mg/dL               |

The FENa is 2.5% and urinalysis shows trace protein and pigment-stained granular casts.

What is most likely responsible for the laboratory findings?

- (A)** Acute tubular necrosis
- (B)** Cirrhosis
- (C)** Alcohol-induced nephropathy
- (D)** Medication
- (E)** UTI

**The answer is A: Acute tubular necrosis.** This case demonstrates the progression of prerenal kidney injury to ATN. While prerenal disease is commonly associated with transient dehydration, other important causes to keep in mind are congestive heart failure and cirrhosis, both of which are likely in this patient. The progression to ATN is evidenced by pigment-stained granular casts classically referred to as “muddy brown” casts.

(B, C) Cirrhosis and alcohol could contribute to prerenal AKI with a fractional excretion of sodium (FENa) <1%. (D) Many medications can cause ATN, including aminoglycosides, iodinated contrast agents, cisplatin, and amphotericin. This is not suggested by the patient’s history. (E) While a UTI is one of the most common causes of confusion in elderly individuals, the urinalysis did not report findings suggestive of infection.

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**69** A 42-year-old man presents to the ED with intermittent right lower abdominal pain described as sharp and radiating to his groin. He has no prior medical problems and has never been hospitalized in the past. His urine dipstick shows trace blood.

Which of the following is the best next step?

- (A) Upright abdominal x-ray
- (B) Abdominal CT with contrast
- (C) Abdominal CT without contrast
- (D) Cystoscopy
- (E) Urine culture

**The answer is C: Abdominal CT without contrast.** Symptoms of unilateral abdominal pain radiating to the groin are consistent with a diagnosis of nephrolithiasis, which is also supported by positive blood on urinalysis. (A) The proper diagnostic test for nephrolithiasis is a CT scan without contrast as this will allow visualization of small or radiolucent stones such as uric acid stones that would not be seen on x-ray. (B, D) CT with contrast and cystoscopy are part of the workup of microscopic hematuria to evaluate for renal cancer and bladder cancer, respectively. However, the patient’s symptoms suggest nephrolithiasis and he can avoid the full workup at this time. (E) This patient does not have symptoms/signs concerning for a UTI.

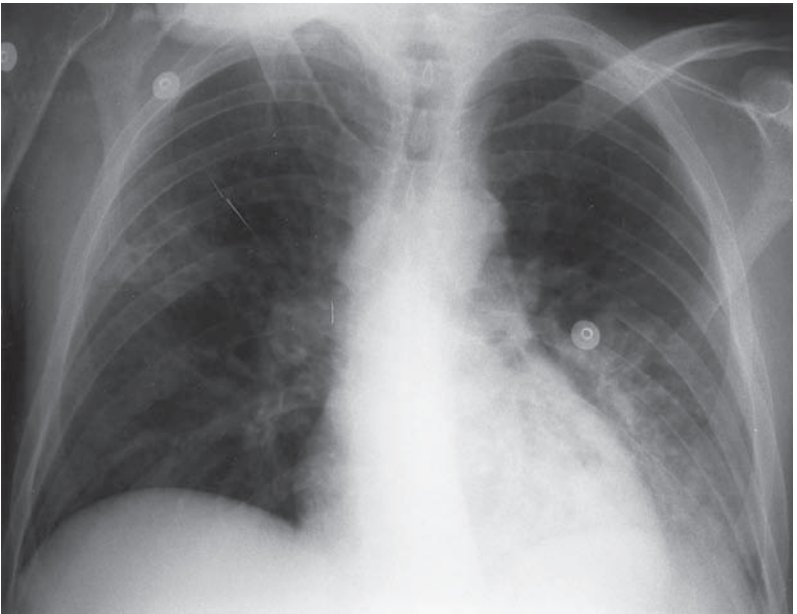
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**70** A 35-year-old man presents with increasing dyspnea and a nonproductive cough over the last week. Vital signs show a temperature of 38.6°C, blood pressure of 110/82 mmHg, heart rate of 112 beats per minute, and an oxygen saturation of 91%. He has a history of HIV infection and is currently not taking any medications. A chest x-ray



is performed (*Figure 12-12*), and his laboratory values are shown below.

|                    |                                          |
|--------------------|------------------------------------------|
| Sodium             | 141 mEq/L                                |
| Potassium          | 3.6 mEq/L                                |
| Bicarbonate        | 25 mEq/L                                 |
| Lactate            | 2.5 mmol/L (normal range 0.6–2.3 mmol/L) |
| Arterial blood gas |                                          |
| pH                 | 7.46                                     |
| pO <sub>2</sub>    | 66 mmHg                                  |
| pCO <sub>2</sub>   | 29 mmHg                                  |



**Figure 12-12**

The patient has a CD4 count of  $13/\text{mm}^3$  and a calculated A–a gradient of 47.

Which of the following is the most appropriate initial treatment?

- (A) Trimethoprim–sulfamethoxazole with prednisone
- (B) Tenofovir/emtricitabine and raltegravir
- (C) Isoniazid, rifampin, ethambutol, and pyrazinamide
- (D) Vancomycin and piperacillin/tazobactam
- (E) Trimethoprim–sulfamethoxazole without prednisone

**The answer is A: Trimethoprim–sulfamethoxazole with prednisone.**

Trimethoprim–sulfamethoxazole is the treatment for PCP pneumonia, which occurs in immunocompromised patients (especially HIV positive patients with a CD4 count  $<200$ ). The history, chest x-ray, and elevated lactate are all consistent with PCP pneumonia. (E) When the  $\text{PaO}_2$  is  $<70$  mmHg or the A–a gradient is  $>35$ , prednisone should be given before antibiotics to limit the amount of pulmonary inflammation in response to PCP cell death and lysis. (B) HIV treatment with tenofovir/emtricitabine and raltegravir should not be initiated immediately since immune reconstitution may lead to worsening inflammation and respiratory distress. (C) This patient does not have findings that suggest TB infection. (D) Vancomycin and piperacillin/tazobactam is a broad-spectrum empiric antibiotic regimen; however, the likely diagnosis is PCP pneumonia and thus antibiotics should be tailored to this organism.

71

An 80-year-old woman is admitted to rule out acute coronary syndrome after recurrent episodes of chest pain. She has not seen a doctor in many years, and her only medication is hydrochlorothiazide. Her blood pressure on admission is 188/120 mmHg, and she is started on labetalol. Her pressure mildly improves, and she is given hydralazine for additional control. She is also started on aspirin and rosuvastatin for risk factor modification. She is discharged and returns to clinic 1 month later complaining of muscle and joint pain, which resolves several weeks after discontinuing one of her medications. Enzyme-linked immunosorbent assay (ELISA) testing reveals a positive anti-histone antibody.

What drug caused this effect?

- (A) Labetalol
- (B) Rosuvastatin
- (C) Aspirin
- (D) Interaction between rosuvastatin and hydrochlorothiazide
- (E) Hydralazine
- (F) Interaction between hydralazine and hydrochlorothiazide

**The answer is E: Hydralazine.** This patient has drug-induced lupus, and hydralazine is one of the medications that can cause this effect. Other common drugs that can cause this are procainamide and penicillamine. Up to 5% of

patients who use hydralazine long term will show some signs of drug-induced lupus, most of which will have a positive anti-histone antibody. **(B)** Statin-induced myopathy occurs weeks to months after starting the medication, and will present with myalgias but not usually joint pain.

72

A 49-year-old man with no significant past medical history presents to your clinic for a follow-up after a motor vehicle collision 2 days ago. Immediately after the accident, he presented to the Emergency Department and received a CT scan of his abdomen, revealing an incidental finding of a 1.2-cm right adrenal nodule. He suffered no injuries from the collision and was sent home the same day. On physical examination today, the patient's temperature is 37.0°C, blood pressure is 112/76 mmHg, and heart rate is 66 beats per minute. The rest of the examination is unremarkable. The results from his metabolic panel are shown below.

|                     |           |
|---------------------|-----------|
| Sodium              | 138 mEq/L |
| Potassium           | 3.8 mEq/L |
| Chloride            | 102 mEq/L |
| Bicarbonate         | 24 mEq/L  |
| Blood urea nitrogen | 15 mg/dL  |
| Creatinine          | 1.0 mg/dL |
| Glucose             | 110 mg/dL |

Which of the following tests is unnecessary in the workup of this patient's condition at this time?

- (A)** Plasma aldosterone and renin levels
- (B)** Overnight dexamethasone suppression test
- (C)** Plasma metanephrine levels
- (D)** 24-hour urine fractionated catecholamines and metanephrines

**The answer is A: Plasma aldosterone and renin levels.** Incidental adrenal adenomas are commonly found after CT imaging of the abdomen done for other purposes. History and physical examination in this case are not revealing for a malignancy or hormone hypersecretion. However, certain testing is required to evaluate for potentially functioning adenomas that secrete cortisol (Cushing syndrome), aldosterone (Conn syndrome), or catecholamines (pheochromocytoma). Given that the patient is not hypertensive and his metabolic panel does not show hypernatremia or hypokalemia, no further testing

for an aldosterone-secreting tumor is required. **(B, C, D)** All of the remaining tests should be done to rule out a hormone-secreting tumor.

**73** A 23-year-old college senior is brought to the hospital by her friends for confusion. They state she was fine until yesterday, when she started behaving abnormally. The patient has no subjective complaints. Her temperature is 39°C, blood pressure is 118/74 mmHg, heart rate is 100 beats per minute, and respiratory rate is 18 breaths per minute. Physical examination is notable for neck stiffness and a diffuse maculopapular rash. While the hips are flexed at 90 degrees, there is no pain with knee extension; while the patient is supine, there is no hip flexion with passive neck flexion.

What is the most appropriate next step in management for this patient?

- (A)** Lumbar puncture
- (B)** CT scan of the head
- (C)** Draw blood cultures and start empiric IV antibiotics
- (D)** Start acyclovir
- (E)** Start ceftriaxone

**The answer is C: Draw blood cultures and start empiric IV antibiotics.**

This patient likely has meningococcal meningitis. The complete triad of fever, neck stiffness, and headache are rarely found; however, two of three signs is 95% sensitive for a diagnosis of meningitis. Kernig and Brudzinski signs are typically late presentations and are not sensitive tests. Given the high mortality rate of meningitis, empiric antibiotics should not be delayed. **(A)** Studies have shown that lumbar puncture can be performed within 2 to 4 hours of starting antibiotics without altering CSF studies. **(B)** CT scan of the head should be performed before lumbar puncture if the patient is at risk of cerebral herniation (e.g., papilledema on physical examination). **(D)** Acyclovir should be started if HSV encephalitis is suspected. **(E)** Ceftriaxone alone is not appropriate empiric antibiotic coverage. Although meningococcal meningitis is suspected, resistant *Streptococcus pneumoniae* should still be covered with vancomycin. If this patient were older than 50, *Listeria* should be covered with ampicillin.

**74** A 71-year-old man complains of fever and back pain. He lives in a skilled nursing facility and has no recent sick contacts or animal exposures. On examination, his temperature is 38.4°C, blood pressure is 148/92 mmHg, heart rate is 106 beats per minute, respiratory rate is 18 breaths per minute, and oxygen saturation is 99% on room air. He has diffuse abdominal pain with voluntary guarding, and has significant pain with right hip flexion. A neurologic examination of the lower

extremities is normal. A CT scan of the abdomen is performed and shows a left psoas abscess.

Which of the following organisms is most likely responsible?

- (A) *Mycobacterium tuberculosis*
- (B) *Pseudomonas aeruginosa*
- (C) *Escherichia coli*
- (D) *Staphylococcus aureus*

**The answer is D: *Staphylococcus aureus*.** The most common cause of a psoas abscess is *S. aureus*, and therefore empiric antibiotics should be directed at this organism. (A) In patients with significant risk factors or from an endemic area, TB should be expected (especially if there is vertebral osteomyelitis and other evidence of disseminated disease). (B, C) Although *Pseudomonas* and *E. coli* may cause these abscesses, they are much less common than *S. aureus*.

75

A 56-year-old man presents with a fever and a productive cough. His previous medical history is unremarkable, and he takes no medications. He is homeless and has been in jail several times. He has a 15 pack-year smoking history and drinks alcohol heavily. Review of systems is remarkable for intermittent fevers, night sweats, and weight loss. On examination, his temperature is 38.9°C and his respiratory rate is 26 breaths per minute. There is dullness to percussion along the right lower lung field with decreased breath sounds over this area on auscultation; the rest of the pulmonary examination is normal. His laboratory values are significant for a hemoglobin of 10.2 g/dL.

Which of the following is the most likely diagnosis?

- (A) *Klebsiella pneumoniae*
- (B) Tuberculous pleural effusion
- (C) Hodgkin lymphoma
- (D) Congestive heart failure
- (E) Malnutrition

**The answer is B: Tuberculous pleural effusion.** Risk factors for TB include immigrants from endemic areas, homelessness, exposure to prisons, health care workers, HIV infection, and exposure to infected individuals, among others. This patient has risk factors in addition to fever, cough, night sweats, and physical examination findings suggestive of a pleural effusion, making TB a potential diagnosis that should not be missed. (A) Community-acquired pneumonia due to *Klebsiella* is seen more often in alcoholics, and it is possible that this patient has pneumonia with a parapneumonic effusion; however, TB should be suspected based on the risk factors and symptoms. In addition, anemia is a sensitive finding in TB. (C) A pulmonary infection should be suspected over Hodgkin lymphoma given the presence of cough. Of note,

lymphoma can present with “B symptoms” that include fevers, night sweats, and so forth. (D) Congestive heart failure causes a transudative effusion, which would not present with fever, night sweats, and so forth. (E) Malnutrition (folate, vitamin B<sub>12</sub>) as well as alcoholism can cause a macrocytic anemia; however, this patient’s anemia is due to TB.

76

A 39-year-old woman arrives at the hospital after her third episode of dizziness. Her first episode was 6 months ago and her most recent episode occurred yesterday. She describes feeling as if the room was spinning around her. During each of these episodes she has experienced significant nausea, often accompanied by emesis. Upon further questioning she tells you that she has been hearing a low rumbling noise in her right ear.

What test is required to confirm your diagnosis?

- (A) CT head
- (B) MRI head
- (C) Audiogram
- (D) Tilt table test
- (E) No need for further testing

**The answer is C: Audiogram.** This patient is experiencing vertigo and tinnitus as evidenced by her episodes of spinning sensation and low rumbling noise in her right ear. These are two of the three main clinical signs of Meniere disease, an autosomal dominant condition that is characterized by episodic vertigo, tinnitus, and sensorineural hearing loss. A definite diagnosis requires all three features, so the next step should be an audiogram to test for sensorineural hearing loss. (A, B) A CT or MRI head does not play a diagnostic role in the evaluation of Meniere disease. (D) A tilt table test may be used in the evaluation of suspected neurocardiogenic syncope.

77

A 56-year-old woman is hospitalized for an asthma exacerbation. She is treated with continuous nebulized ipratropium and albuterol. She recovers without complications and is discharged. Upon questioning she states that she currently uses an albuterol inhaler nearly every day and a daily low-dose inhaled corticosteroid. She states that she wakes up about one to two times per week in the middle of the night due to her asthma. Pulmonary function tests reveal a FEV<sub>1</sub> of 75%.

What is the best pharmacologic addition for the management of her asthma?

- (A) Begin a daily oral corticosteroid
- (B) Begin a long-acting  $\beta$ -agonist
- (C) Begin a high-dose inhaled corticosteroid
- (D) Begin theophylline
- (E) Begin omalizumab

**The answer is B: Begin a long-acting  $\beta$ -agonist.** This patient has moderate persistent asthma based on her frequency of symptoms and her FEV<sub>1</sub>. The best management option is to step up her asthma therapy, and there are two options: add a long-acting  $\beta$ -agonist to her regimen, or increase her low-dose inhaled corticosteroid to a medium-dose inhaled corticosteroid. (A) Oral corticosteroids are a last resort if symptoms fail to improve with a long-acting  $\beta$ -agonist and a high-dose inhaled corticosteroid. (C) The next step would be a medium-dose, not high-dose, inhaled corticosteroid. (D, E) Theophylline and omalizumab are used as alternative agents but are not first-line treatment options in step-up therapy.

78

A 38-year-old IV drug abuser comes to the Emergency Department with a 3-day history of low-grade fevers and pleuritic chest pain. On examination, he has nail bed hemorrhages, nontender ecchymotic lesions on the palms (Figure 12-13), small petechiae on the palatal mucosa, and a right-sided diastolic murmur. He has no focal neurologic deficit.



**Figure 12-13**

Which of the following should be done urgently for this patient?

- (A) Begin vancomycin
- (B) Check liver enzymes
- (C) Begin a  $\beta$ -blocker
- (D) CT chest with contrast
- (E) Begin ceftriaxone and gentamicin

**The answer is A: Begin vancomycin.** This patient is presenting with acute bacterial endocarditis, which is often caused by gram-positive organisms (especially *S. aureus* in IV drug users). The figure above shows Janeway lesions as a result of septic emboli. The appropriate empiric treatment, after blood cultures

are sent, is to immediately begin vancomycin since it will cover *S. aureus* (and MRSA). (E) Ceftriaxone and gentamicin are used empirically to treat subacute bacterial endocarditis. (B, C) This patient does not have liver or heart failure. (D) A CT chest with contrast may be used to diagnose pulmonary embolism. Septic emboli to the lungs may be present if the patient has a right-sided vegetation; however, this diagnostic test is not indicated as part of the workup.

79

A 59-year-old man is admitted for an acute flare of his chronic tophaceous gout and is found to be anemic with a hemoglobin of 8.9 g/dL. Additional studies show a mean corpuscular volume of  $75 \mu\text{m}^3$ , a serum ferritin of 14 ng/mL, and a serum iron of 35  $\mu\text{g/dL}$ . He is hemodynamically stable and denies any hematochezia or melena.

Which of the following is the best next step?

- (A) Emergent inpatient colonoscopy
- (B) Transfuse 1 unit packed red blood cells
- (C) Repeat complete blood count and iron studies in 1 week
- (D) Outpatient colonoscopy

**The answer is D: Outpatient colonoscopy.** This patient has a microcytic anemia with low ferritin and low iron levels that is consistent with iron-deficiency anemia. All patients should receive a screening colonoscopy at the age of 50; however, this patient has an additional reason for having a colonoscopy—all patients older than 50 with microcytic anemia in the absence of any obvious blood loss is a red flag for colorectal cancer. (A) The patient is hemodynamically stable without any signs of active GI bleeding and therefore does not require an emergent inpatient colonoscopy. (B) A conservative approach to blood transfusion is the best option in this stable patient, and his hemoglobin is not low enough to warrant transfusion. (C) While repeating a CBC to ensure that his hemoglobin is not rapidly dropping may be a good idea; there is no value in repeating iron studies in 1 week.

80

A 29-year-old Caucasian man presents with fever and foot pain 4 days after he stepped on a nail while exercising on an outdoor track. Examination reveals a deep tissue abscess at the puncture site. No crepitus is noted. Laboratory studies reveal leukocytosis and an ESR of 120 mm/h. The patient is up-to-date on all vaccinations.

After surgical debridement of the injury, antibiotic therapy should be chosen to best cover which of the following pathogens?

- (A) *Clostridium tetani*
- (B) *Pseudomonas aeruginosa*
- (C) *Streptococcus pyogenes*
- (D) *Mycobacterium avium* complex (MAC)
- (E) *Salmonella typhi*



**The answer is B: *Pseudomonas aeruginosa*.** *Pseudomonas aeruginosa* is a common cause of osteomyelitis following nail puncture, especially in people wearing tennis shoes. (A) The patient is not exhibiting symptoms of tetanus (muscle spasms, trismus, risus sardonicus, opisthotonos, etc.), which is primarily managed with tetanus immune globulin in unvaccinated patients. (C) The patient examination and mechanism of injury is less suggestive of *S. pyogenes* infection, though this is a common cause of cellulitis. (D) MAC infection is associated with HIV and is unlikely to be the cause of this patient's osteomyelitis. (E) Salmonella osteomyelitis is associated with sickle cell disease.

81

A 45-year-old obese woman with a history of obstructive sleep apnea and obesity hypoventilation syndrome presents with worsening shortness of breath. She is afebrile and requires supplemental oxygen. On examination, she has a right-sided heave with a loud S2 and a systolic murmur along the right sternal border. Her liver is pulsatile. The patient is admitted and a right heart catheterization is performed.

Which of the following best represents the likely findings during this procedure? (Note: LVEF is left ventricular ejection fraction, RAP is right atrial pressure, PAP is mean pulmonary artery pressure, PCWP is pulmonary capillary wedge pressure.)

|     | LVEF   | RAP | PAP | PCWP   |
|-----|--------|-----|-----|--------|
| (A) | Normal | ↑   | ↑   | Normal |
| (B) | ↓      | ↑   | ↓   | ↓      |
| (C) | Normal | ↓   | ↓   | ↑      |
| (D) | ↓      | ↑   | ↑   | ↑      |

**The answer is A: Normal LVEF, ↑ RAP, ↑ PAP, normal PCWP.** In patients with chronic hypoxemia (obstructive sleep apnea, obesity hypoventilation syndrome), there is an increased risk of pulmonary hypertension; therefore, treatment of these underlying conditions is essential to prevent this, since pulmonary hypertension has a high morbidity and mortality. The findings on examination support that this patient has right heart failure. Because the primary problem is hypertension in the pulmonary arteries, the PCWP (equivalent to the left atrial pressure) will be normal, and LVEF will often be normal as long as the left ventricle gets sufficient preload.

82

A 22-year-old African American woman presents for evaluation of scars on her earlobes. The patient reports that 1 year ago she had her ears pierced. Since the piercing, her ear lobes have not healed and have formed large scars that are itchy and painful. Physical examination

reveals excessive scar tissue on the left and right earlobes. Both earlobes are tender to palpation.

Which of the following is the best treatment for this condition?

- (A) Surgical excision
- (B) Cryosurgery
- (C) Intralesional corticosteroids
- (D) Topical corticosteroids
- (E) Removal of all nickel-containing jewelry

**The answer is C: Intralesional corticosteroids.** This patient is presenting with keloids on her bilateral earlobes. Keloids are benign fibrous growths that develop in scar tissue and result from excessive extracellular matrix and dermal fibroblast production. Keloids can be painful and are more common in African American patients. The best way of treating keloids is with intralesional corticosteroids. (A) There is a high rate of recurrence with surgical excision, though the earlobes often have a lower rate of recurrence. (B, D) Cryosurgery and topical corticosteroids are not effective. (E) Nickel allergies are common and can cause severe erythema and swelling. Excessive scar tissue that extends beyond the site of original trauma is by definition a keloid (vs. a hypertrophic scar, in which there is excessive scar tissue limited to the site of trauma).

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83

A 51-year-old man presents with fever, chills, productive cough, and wheezing. The patient also endorses night sweats. His is diagnosed with pneumonia and started on a fluoroquinolone antibiotic. Two of his sputum samples are positive for acid-fast bacilli (AFB). The nurses are concerned about their exposure to this patient.

Which of the following is the best course of action for individuals exposed to TB?

- (A) Chest x-ray in 3 months
- (B) Begin treatment with isoniazid
- (C) Place PPD now and repeat in 3 months
- (D) Take chest x-ray now and place PPD in 3 months

**The answer is C: Place PPD now and repeat in 3 months.** It is recommended by the Center for Disease Control (CDC) that all health care workers who are exposed to a contagious patient with TB immediately receive a PPD test. If negative, the PPD test is repeated in 3 months to monitor any change in status that might have occurred from exposure to TB.

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84

A 65-year-old man undergoes a right carotid endarterectomy for a 90% stenosis. Four months following surgery, carotid ultrasound demonstrates 40% stenosis of the right internal carotid.

What is the most likely etiology of the restenosis?

- (A) Atherosclerotic disease
- (B) Endothelial hyperplasia
- (C) Hyaline arteriosclerosis
- (D) Vasospasm

**The answer is B: Endothelial hyperplasia.** Endothelial hyperplasia is a common cause of early re-stenosis following carotid endarterectomy, and this often regresses over time. (A) Redevelopment of atherosclerotic disease in such a short time frame would be unlikely. (C) Hyaline arteriosclerosis is associated with hypertension. (D) Vasospasm is a complication of filter devices placed during the procedure, but is unlikely to occur after the procedure.

85

A 34-year-old man presents with a low-grade fever, chest pain, and dyspnea. A few days ago he states that he felt fatigued and had myalgias. He has no past medical history. A chest radiograph shows a widened mediastinum.

What is the most likely diagnosis?

- (A) Influenza
- (B) Pulmonary embolism
- (C) Anthrax
- (D) Aortic dissection
- (E) Pneumothorax

**The answer is C: Anthrax.** The respiratory symptoms and a widened mediastinum on chest radiograph make pulmonary anthrax the most likely diagnosis. This disease progresses from flu-like symptoms to mediastinitis and pulmonary hemorrhage. (A, B) Influenza and pulmonary embolism would not produce a widened mediastinum on chest x-ray. (D) Aortic dissection produces a widened mediastinum on chest x-ray, but the patient is young without any obvious risk factors, and the presence of fever also makes this less likely. (E) A pneumothorax would be seen on chest x-ray.

86

A 46-year-old man presents to the Emergency Department with headache and confusion. His medical history is significant for diabetes mellitus and chronic liver disease. Physical examination reveals a temperature of 39.3°C, nuchal rigidity, and dark skin pigmentation. He is admitted and a lumbar puncture is performed. The results of CSF analysis are shown below.

|               |                                                   |
|---------------|---------------------------------------------------|
| Leukocytes    | 110/mm <sup>3</sup> (predominance of lymphocytes) |
| Total protein | 104 mg/dL                                         |
| Glucose       | 24 mg/dL                                          |

A gram stain of the CSF is negative.

Which of the following is likely responsible for this patient's symptoms?

- (A) Herpes simplex virus
- (B) *Haemophilus influenzae*
- (C) *Staphylococcus aureus*
- (D) *Cryptococcus neoformans*
- (E) *Mycobacterium tuberculosis*
- (F) *Listeria monocytogenes*
- (G) Human immunodeficiency virus
- (H) *Neisseria meningitidis*

**The answer is F: *Listeria monocytogenes*.** The history of diabetes and liver failure with darkened skin on examination should raise suspicion for hemochromatosis, which commonly presents around this age in men. Patients with iron overload disorder are at higher risk of iron-loving organisms (e.g., *Listeria*, *Vibrio vulnificus*), and so meningitis should raise concern for this organism. The CSF findings are consistent with bacterial meningitis (low glucose and high protein), and like TB it can cause a lymphocytic pleocytosis. Because *Listeria* is an intracellular organism, gram staining is often negative; if positive, it will show gram-positive rods. The empiric antibiotic regimen for this patient should therefore include ampicillin to cover *Listeria meningitis*.

87

A 67-year-old man comes to the hospital after fainting while jogging. This was the first time this has happened, although he has been feeling dizzy and short of breath during exercise for the past several months. ECG shows left ventricular hypertrophy, and an echocardiogram shows extensive calcification of the aortic valve. He is subsequently scheduled for a valve replacement.

What other study should be ordered prior to surgery?

- (A) Exercise stress test
- (B) Coronary angiography
- (C) Pharmacologic stress test
- (D) Electroencephalogram (EEG)
- (E) Functional MRI of the brain

**The answer is B: Coronary angiography.** Prior to aortic valve replacement surgery, every patient should have his or her coronary arteries evaluated in case there is a need for CABG at the same time as the valve replacement surgery. (A, C) Cardiac stress testing would be helpful in diagnosing coronary artery disease, but the standard of care for an aortic valve replacement is to bypass the stress test in favor of angiography due to its superior accuracy. (D, E) The patient's symptoms can be attributed to his valvular disease rather than a neurologic process.

88

A 52-year-old man presents to his primary care physician complaining of painful red bumps on his legs and muscle pain. On review of systems, the patient endorses weight loss over the last few months due to abdominal pain after eating. He has also noticed a slight limp. Physical examination is notable for erythematous tender nodules and palpable purpuric lesions predominantly over his lower extremity as well as a reticulated pattern of skin discoloration. He has a small decrease in strength and sensation in his right foot compared to his left.

Which of the following tests should be performed next to best identify the cause of this patient's symptoms?

- (A) ANCA antibody test
- (B) Serum blood urea nitrogen to creatinine ratio
- (C) Erythrocyte sedimentation rate
- (D) Tissue biopsy of skin lesions
- (E) Chest x-ray

**The answer is D: Tissue biopsy of skin lesions.** This patient presents with symptoms of polyarteritis nodosa (PAN), which is diagnosed with a biopsy of an involved organ. (A) A positive ANCA is unlikely to be found in PAN and suggests an ANCA-positive vasculitis. (B, C) Although serum BUN to creatinine ratio and ESR are likely to be abnormal in patients with PAN, these tests are not specific. (E) A chest x-ray is used to rule out PAN as lung involvement is rare and positive findings suggest a different vasculitis.

89

A 23-year-old woman presents to the clinic with complaints of vague joint pains and a chronic rash on her face for the last year. She does not take any medications and uses no vitamins or supplements. She denies any known allergies. On examination, her temperature is 37.0°C, blood pressure is 130/80 mmHg, and heart rate is 70 beats per minute. Raised and scar-like circular red plaques are visible on her nasal bridge, pinnae, and neck in various stages of resolution. There is visible scarring and depigmentation in the central area of most lesions with a peripheral rim of hyperpigmentation. Her laboratory results are shown below.

|                 |                        |
|-----------------|------------------------|
| Hemoglobin      | 10.0 g/dL              |
| Leukocyte count | 2,500/mm <sup>3</sup>  |
| Platelets       | 70,000/mm <sup>3</sup> |
| ANA             | Positive               |

Which of the following tests is most likely to be positive in this patient?

- (A) HIV test
- (B) Anti-smooth muscle antibody
- (C) Anti-histone antibody
- (D) Anti-centromere antibody
- (E) Rapid plasma reagin (RPR)
- (F) Heterophile antibody test
- (G) Osmotic fragility test

**The answer is E: RPR.** This question describes the discoid rash of SLE. This rash, in addition to vague joint pains, anemia, thrombocytopenia, leukopenia, and a positive ANA, makes SLE the most likely diagnosis. SLE is typically confirmed with the anti-dsDNA antibody or anti-Smith antibody. RPR and FTA/VDRL, which are tests for syphilis infection, are often positive in SLE. (A) The presentation and positive ANA indicate SLE, not HIV infection. (B, F, G) Anti-smooth muscle antibodies (for autoimmune hepatitis), the heterophile antibody test (for EBV infection), and the osmotic fragility test (for hereditary spherocytosis) would be unlikely to be positive in this patient. (C) Drug-induced lupus is confirmed with positive anti-histone antibodies; however, this patient does not take any medications. (D) Anti-centromere antibodies are often seen in limited systemic sclerosis (CREST syndrome).

90

A 48-year-old woman presents with a rash (*Figure 12-14*) and progressive difficulty in reaching for objects in cabinets and lifting her arms to brush her hair. Laboratory values indicate a creatine kinase (CK) of 1,400 U/L.



**Figure 12-14**

In addition to corticosteroids, what is the most appropriate next step in management?

- (A) Genetic testing
- (B) Screen for malignancy
- (C) Detailed history of toxic exposures
- (D) Search for infectious cause
- (E) No further tests indicated

**The answer is B: Screen for malignancy.** This patient's presentation is consistent with dermatomyositis, which may present as a paraneoplastic syndrome. Both patients with dermatomyositis and polymyositis typically present with symmetrical proximal muscle weakness most commonly involving the shoulders but may also involve the pelvic muscles (difficulty rising from a chair). They both may have elevated CK, positive ANA, or positive anti-Jo-1 antibodies. However, patients with dermatomyositis will also present with a dermatologic finding such as a heliotrope rash, malar rash, or Gottron papules (*Figure 12-11*). Muscle biopsy will demonstrate perifascicular atrophy. Though there is an association with malignancy in both dermatomyositis and polymyositis, the risk is greater with dermatomyositis.



A 62-year-old woman with a history of alcoholism and homelessness presents to the Emergency Department because of abdominal pain. She has not been to the doctor in years and does not take any medications, herbs, or supplements. She is afebrile but is jaundiced with abdominal distention, pitting edema of the lower extremities, and palmar erythema. Her laboratory values are significant for the following.

|                            |                        |
|----------------------------|------------------------|
| Hemoglobin                 | 10.2 g/dL              |
| Leukocyte count            | 8,300/mm <sup>3</sup>  |
| Platelets                  | 71,000/mm <sup>3</sup> |
| Sodium                     | 131 mEq/L              |
| Creatinine                 | 1.8 mg/dL              |
| Albumin                    | 1.8 g/dL               |
| Total bilirubin            | 7.0 mg/dL              |
| Direct bilirubin           | 5.4 mg/dL              |
| Aspartate aminotransferase | 74 U/L                 |
| Alanine aminotransferase   | 92 U/L                 |

An ultrasound shows a small, nodular liver. IV fluids are given to the patient but her renal function does not improve.

Which of the following is the underlying mechanism of this patient's renal failure?

- (A) Urinary tract obstruction
- (B) Neoplastic invasion
- (C) Toxic insult
- (D) Afferent arteriole vasodilation
- (E) Splanchnic vasodilation

**The answer is E: Splanchnic vasodilation.** The patient has physical examination findings, laboratory values, and an ultrasound consistent with cirrhosis of the liver, likely from alcohol abuse. She also has poor renal function, which is called hepatorenal syndrome and portends a poor prognosis. The mechanism of renal failure in liver cirrhosis is caused by splanchnic vasodilation in response to portal hypertension. This produces a decrease in systemic vascular resistance and blood pressure, leading to decreased effective circulating volume and an increase in angiotensin II and norepinephrine, leading to renal afferent arteriole vasoconstriction and renal ischemia. (D) Afferent arteriole vasodilation would increase renal blood flow and be beneficial. (A) Cirrhosis does not cause bilateral urinary tract obstructions. (B) Patients with cirrhosis are at an increased risk of hepatocellular carcinoma; however, there are no further clues in the vignette that this patient has cancer. (C) The patient denied any medications, herbs, or supplements.

92

A 41-year-old man presents for a routine health maintenance examination. The patient has no complaints other than a “nagging cough” for the past 2 weeks. He has a history of hypertension and diabetes and has smoked one pack of cigarettes per day for the last 15 years. His mother was diagnosed with colon cancer at the age of 52. Physical examination and routine laboratory values are all within normal limits.

Which of the following is the most appropriate step for this patient?

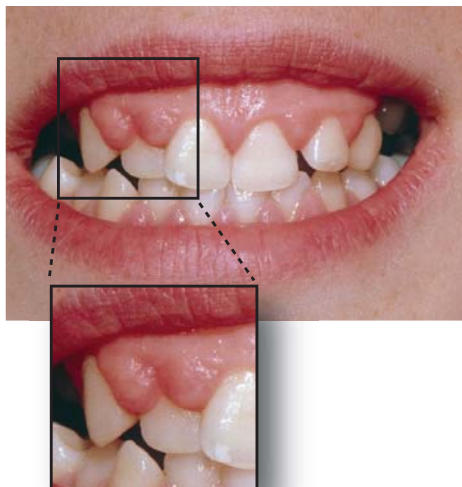
- (A) Colonoscopy now
- (B) Colonoscopy in 1 year
- (C) Colonoscopy at the age of 45
- (D) Colonoscopy at the age of 50

**The answer is A: Colonoscopy now.** This patient is considered high risk for colorectal cancer as he has a first-degree relative with colorectal cancer (mother) before the age of 60. Two or more first-degree relatives with colorectal cancer at *any* age is also considered high risk. *High-risk* patients should be screened for colon cancer at the age of 40 or 10 years before the relative's diagnosis (*choose the one that comes first*). In this patient, his mother was diagnosed with colon cancer at the age of 52, and since the patient is 41 years old, he should be screened today instead of 1 year at the age of 42. Of note, it is helpful to remember that in the outpatient setting, the most common causes of a chronic cough are asthma, GERD, and postnasal drip.



93

A 39-year-old man with a history of HSV encephalitis is brought into the hospital after experiencing a seizure that lasted several minutes. Further history reveals that this has happened several times previously. He is started on a medication and discharged. Several months later, the patient follows up and has the findings shown below (*Figure 12-15*).



**Figure 12-15**

Which of the following medications is most likely responsible?

- (A) Lorazepam
- (B) Valproic acid
- (C) Phenytoin
- (D) Phenobarbital

**The answer is C: Phenytoin.** This patient has gingival hyperplasia, a well-known side effect of phenytoin. (B, D) Many anticonvulsants are also associated with gingival hyperplasia; however, the risk is greatest with phenytoin. Other medications that can cause this are cyclosporine and calcium channel blockers. (A) Lorazepam is a benzodiazepine that is used in the treatment of status epilepticus; however, it is not used for chronic seizure prophylaxis.

94

A 23-year-old college student is brought in by police to the Emergency Department in the middle of the night. He was found running down the street screaming, and is now extremely irritable and holding his chest. A full history cannot be obtained due to the patient's altered

mental status. On examination, he is hyperactive and diaphoretic, and old needle tracks are seen on his arms. His vitals show a temperature of 38.1°C, blood pressure of 154/92 mmHg, heart rate of 154 beats per minute, and respiratory rate of 18 breaths per minute. He has marked mydriasis. An ECG shows ST depression and T wave inversions in multiple leads. Urine toxicology screen and initial laboratory values are ordered.

Which of the following should NOT be given to the patient at this time?

- (A) Aspirin
- (B) Lorazepam
- (C) Metoprolol
- (D) Diltiazem
- (E) IV fluids
- (F) Nitroglycerin

**The answer is C: Metoprolol.** This patient is acutely intoxicated with cocaine (sympathetic hyperactivity, dilated pupils) and there is concern for cocaine-induced myocardial ischemia given that the patient was holding his chest and an ECG was consistent with ischemia. Cocaine blocks dopamine reuptake in the central nervous system, causing euphoria, but also blocks norepinephrine reuptake in sympathetic neurons and produces many of the sympathomimetic signs seen in this patient. The cardiovascular effects include myocardial infarction and arrhythmias and therefore it is important to consider these life-threatening consequences in patients who abuse cocaine. All of the options above are appropriate for a patient presenting with chest pain after cocaine use, except for metoprolol. Theoretically,  $\beta$ -blockers should be avoided while cocaine is still present in the body, since  $\beta$ -blockade can result in unopposed  $\alpha$ -receptor activation leading to worsening hypertension and coronary vasospasm. Though the clinical significance of this problem is debated (recent data suggests that  $\beta$ -blockers are likely safe in this setting), it is a widely taught principle and may still show up on the shelf examination. This is also important to remember for other conditions that cause very elevated sympathetic activity (e.g., pheochromocytoma).



95 A 60-year-old woman with a longstanding history of rheumatoid arthritis presents to the Emergency Department with shortness of breath, productive cough, and fever. Chest x-ray shows right lower lobe consolidation, consistent with pneumonia, along with numerous rheumatoid nodules that are unchanged from prior x-rays. Her medical record shows that this is her third hospitalization this year. Laboratory values show a leukocyte count of  $1,200/\text{mm}^3$ , and a diagnosis of Felty syndrome is made.

What additional finding would you expect in this patient?

- (A) Mildly elevated rheumatoid factor titers
- (B) Splenomegaly
- (C) Polycythemia, thrombocytosis, and hyperviscosity
- (D) Lack of response to disease-modifying antirheumatic drugs

**The answer is B: Splenomegaly.** Felty syndrome is characterized by the triad of rheumatoid arthritis, neutropenia, and splenomegaly. It may go misdiagnosed as simply rheumatoid arthritis for many years before laboratory values reveal neutropenia, often found after admission for one of their frequent infections. (A) Rheumatoid factor will be markedly elevated. (C) Patients will also be anemic and thrombocytopenic due to splenic consumption of blood cells and platelets. (D) Patients with Felty syndrome respond well to treatment of the underlying rheumatologic disease.

96

An 18-year-old boy with cystic fibrosis presents to the Emergency Department with a 4-day history of progressively worsening productive cough, fever, and malaise. His temperature is 38.8°C, blood pressure is 110/75 mmHg, heart rate is 104 beats per minute, and respiratory rate is 24 breaths per minute. Chest x-ray demonstrates a right lower lobe infiltrate.

Which antibiotic would be most beneficial for empiric treatment of this patient?

- (A) Vancomycin
- (B) Clindamycin
- (C) Azithromycin
- (D) Piperacillin–tazobactam
- (E) Ceftriaxone
- (F) Trimethoprim–sulfamethoxazole
- (G) Rifampin

**The answer is D: Piperacillin–tazobactam.** Cystic fibrosis patients are particularly susceptible to *Pseudomonas* infections, and the only answer choice that has good coverage of *Pseudomonas* is D. (A) Vancomycin is used for resistant *S. pneumoniae* and MRSA. (B) Clindamycin is useful for anaerobic infections (e.g., aspiration pneumonia). (C) Azithromycin is the antibiotic of choice for outpatient treatment of community-acquired pneumonia (CAP). (E) Ceftriaxone is used for inpatient treatment of pneumonia. (F) Trimethoprim–sulfamethoxazole is used for PCP pneumonia. (G) Rifampin is used for the treatment of TB.

97

A 62-year-old man presents with acute swelling of his left knee. He describes excruciating pain and swelling for the past 2 days. The patient presented with a similar episode 2 years ago, but is unable to recall what

condition he was diagnosed with and what medication he was administered. He has a past medical history of diabetes, hyperlipidemia, hypertension, and chronic alcoholism. He drinks 5 to 6 beers per day. He has a temperature of 38.4°C, blood pressure of 120/80 mmHg, and heart rate of 75 beats per minute. Physical examination reveals a tender and erythematous left knee with significantly limited range of motion and marked swelling.

Which of the following is the best next step in management for this patient?

- (A) Indomethacin
- (B) Joint aspiration with synovial fluid analysis
- (C) Uric acid levels
- (D) Knee x-ray

**The answer is B: Joint aspiration with synovial fluid analysis.** This patient is presenting with signs and symptoms consistent with an acute gout attack. Although unable to recall the exact name of his previous diagnosis, the previous acute episode and patient's alcohol use lend credence to the history of gouty arthritis. Furthermore, the patient is presenting with acute left knee pain, swelling, and low-grade fever, all confirming the likely diagnosis of gout. Given that septic arthritis and pseudogout can show clinical similarities to gout, it is imperative to first perform joint aspiration and synovial fluid analysis. Synovial fluid analysis of gout will demonstrate a leukocyte count of 2,000 to 50,000/mm<sup>3</sup> and negatively birefringent needle-shaped crystals with a negative gram stain and negative culture. (A) Indomethacin (an NSAID) is very helpful in treating acute gout. Nonetheless, the diagnosis of gout must first be confirmed prior to administering indomethacin especially with its side effect profile. (C) Uric acid levels will certainly be elevated in gout (elevated uric acid is the underlying cause of the clinical manifestations); however, uric acid levels do not have a high degree of sensitivity or specificity for diagnosing gout. (D) An x-ray of the knee is not as specific as synovial fluid analysis for diagnosing gout.



98 A 55-year-old woman presents to the office with a 1-week history of dry cough, sore throat, and nasal congestion. She has a 5 pack-year smoking history but successfully quit over 15 years ago. She was diagnosed with asthma as a child and used an albuterol inhaler intermittently, but has not seen a physician or received an inhaler in the last 10 years. The patient's temperature is 36.7°C, blood pressure is 120/80 mmHg, and heart rate is 72 beats per minute. Mild rhinorrhea is present but there are no other significant

examination findings. A chest radiograph is obtained and shown below (*Figure 12-16*).



**Figure 12-16**

What is the best next step in management of this patient?

- (A) Albuterol inhaler
- (B) CT chest
- (C) Azithromycin
- (D) Reassurance
- (E) Rapid strep testing

**The answer is D: Reassurance.** This patient has findings of an upper respiratory infection (URI) including nasal congestion, sore throat, cough, and rhinorrhea. Other common features are sneezing and malaise. The most common pathogens associated with URI include rhinovirus, coronavirus, parainfluenza virus, adenovirus, enterovirus, and RSV. No medications have

been demonstrated to shorten the duration of illness, thus reassurance is the correct answer. (A) An albuterol inhaler or nebulizer would be the appropriate treatment if the patient had an asthma exacerbation. However, the patient's only distant history of asthma and absence of wheezing on lung examination make this diagnosis unlikely. (B) Further evaluation with CT imaging is inappropriate given her normal examination and normal chest radiograph. (C) Azithromycin would be an appropriate answer for a COPD exacerbation; however, her smoking history is minimal and her presenting symptoms lack sputum production or dyspnea. (D) A rapid strep test would be appropriate if the patient met two to three Centor criteria; however, she has a cough without fever, tonsillar exudates, or lymphadenopathy, which gives her a score of zero and makes her risk of streptococcal infection less than 10%.



99 A 45-year-old woman presents to her physician complaining of 3 weeks of fevers and pain in her knees and ankles. She also states that she often wakes up during the night drenched in sweat. On examination, her temperature is 38.1°C, blood pressure is 123/56 mmHg, heart rate is 78 beats per minute, and oxygen saturation is 98% on room air. She has 1+ radial pulses, 2+ dorsalis pedis pulses, and mild decreased range of motion in her bilateral knees secondary to pain.

Which of the following is the most appropriate next step in management?

- (A) Methotrexate
- (B) Prednisone
- (C) Endovascular aortic stent placement
- (D) Ceftriaxone
- (E) Genetic screening

**The answer is B: Prednisone.** The patient's age and symptoms are consistent with Takayasu arteritis, a large vessel vasculitis defined by granulomatous thickening of the aortic arch and proximal great vessels. Corticosteroids are the preferred treatment. (A) Methotrexate is a treatment for rheumatoid arthritis, which may present with arthritis and low-grade fevers; however, this would not explain the discrepancy between her upper and lower extremity pulses. (C) Endovascular stent placement would be considered if there was concern for coarctation of the aorta. However, coarctation of the aorta (associated with Turner syndrome) has the opposite findings from our patient, showing a decreased blood pressure in the lower extremities with hypertension in the upper extremities. There is also delayed femoral pulses (brachial-femoral delay). (D) Ceftriaxone would be an appropriate treatment for gonococcal arthritis; however, this diagnosis would not produce the difference in upper and lower extremity pulses.

100

A 47-year-old woman presents to the clinic complaining of headache and nasal discharge. She says that this has happened to her many times before, and it goes away with antibiotics. She also mentions that her urine has been unusually dark for the past few days. On examination, a saddle nose deformity is noted. A urinalysis is performed and shows significant blood with red blood cell casts.

What is the most likely diagnosis?

- (A) Goodpasture syndrome
- (B) Poststreptococcal glomerulonephritis
- (C) Granulomatosis with polyangiitis
- (D) Congenital syphilis

**The answer is C: Granulomatosis with polyangiitis.** Formerly known as Wegener granulomatosis, this necrotizing small vasculitis often presents with recurrent sinusitis, pulmonary involvement (infiltrates/nodules on chest x-ray, hemoptysis), and renal involvement (rapidly progressive glomerulonephritis). Testing for c-ANCA should be performed, and the patient should receive immunosuppressive agents (steroids + rituximab or cyclosporine). This patient has sinusitis with a nephritic syndrome, making this a concerning diagnosis. (A) Goodpasture syndrome often presents with pulmonary and renal involvement; however, the recurrent sinusitis and saddle nose deformity seen in this patient suggests granulomatosis with polyangiitis. (B) Poststreptococcal glomerulonephritis is a common cause of the nephritic syndrome; however, it occurs a couple of weeks after a group A strep infection (throat or skin) and would not occur concurrently with sinusitis. (D) Congenital syphilis can also produce a saddle nose deformity, but it would not cause recurrent sinusitis and glomerulonephritis.





## Shelf Pearls

*The goal of this chapter is to provide a quick review of high-yield information that should be read prior to taking the shelf examination. It is meant to be a concise summary with an appropriate amount of detail for the examination, and not an exhaustive list of every detail that could show up on the examination.*

### Cardiology

*The topic of cardiovascular disorders makes up a large portion of the shelf examination (around 15% to 20% of questions, according to the NBME). It is important to understand the pathophysiology of the most common diseases that show up on the examination, as well as how to diagnose and treat these diseases (with some exceptions, outlined below). Another good use of your time would be to learn the common medications used to treat these diseases, and to know the most common and most dangerous adverse reactions.*

#### **I. Acute Coronary Syndrome (ACS): unstable angina, non-ST elevation myocardial infarction (NSTEMI), ST elevation myocardial infarction (STEMI)**

##### **A. Definitions**

1. Stable angina (not ACS) typically lasts 10 to 15 minutes, occurs after exertion, relieved with rest or nitroglycerin
2. Unstable angina: angina that is new onset, crescendo, or at rest, typically lasts <30 minutes; subtotal coronary thrombosis; +/- ECG changes (ST depression, T wave inversion); troponin/CK-MB (-)
3. NSTEMI: same as unstable angina but troponin/CK-MB (+)
4. STEMI: typically angina at rest lasting >30 minutes, total coronary thrombosis; ECG shows ST elevations; troponin/CK-MB (+)

##### **B. Diagnosis**

1. Symptoms/signs: retrosternal chest pain/pressure (nonpleuritic) radiating to left arm/jaw, diaphoresis, nausea, dyspnea; beware silent MIs, especially in diabetics (due to neuropathy)
2. Troponin/CK-MB will differentiate UA from NSTEMI and STEMI, ECG will differentiate NSTEMI from STEMI
3. May show ECG on shelf with obvious ST elevation if STEMI; look for localization (Table 13-1); if diffuse ST elevations, think pericarditis

**Table 13-1 ECG Findings in Myocardial Infarction**

| MI Location  | Affected Artery  | Leads                      |
|--------------|------------------|----------------------------|
| Anteroseptal | LAD              | V1–V4                      |
| Apical       | LAD, LCx, or RCA | V5–V6                      |
| Lateral      | LCx              | I, aVL                     |
| Inferior     | RCA >LCx         | II, III, aVF               |
| Posterior    | RCA or LCx       | ST depressions V1–V3       |
| RV infarct   | RCA              | V1–V2, V4R (reverse leads) |

LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery.

**C. Treatment**

1. All patients
  - a. **MONA**: Morphine, O<sub>2</sub>, Nitroglycerin, aspirin (ASA); ASA and nitroglycerin most important, morphine and O<sub>2</sub> for persistent symptoms
  - b. Dual antiplatelet agent (e.g., clopidogrel), heparin,  $\beta$ -blocker (unless hypotensive), statin;  $\beta$ -blocker and statin should be given early, other medications (e.g., ACE inhibitor) can wait
2. For NSTEMI and STEMI: catheterization laboratory if available or fibrinolytics
  - a. Goals: percutaneous coronary intervention (PCI) within 90 minutes, or fibrinolytic within 30 minutes (PCI favored, so short transfers to center with catheterization laboratory preferred)
3. Coronary artery bypass graft (CABG) versus PCI: do not need to know specific details, but PCI is usually the answer; CABG has better outcomes in DM, three vessel disease, left main disease
4. Right ventricular (RV) infarct: preload dependent, so do not give anything that reduces preload (e.g., nitroglycerin); give fluids!
5. Discharge medicines, **AABBCCDE**: ASA, ACE inhibitor (ACEI) or angiotensin receptor blocker (ARB),  $\beta$ -Blocker, Clopidogrel, Cholesterol (statin), Diet, Exercise

**D. Post-MI Complications**

1. Patient develops worsening shortness of breath (SOB) with rales and peripheral edema on examination: congestive heart failure (CHF)
2. Patient complains of dizziness and has bradycardia: heart block (can develop rapidly)
  - a. Look for any other arrhythmia post-MI: atrial fibrillation (a-fib), ventricular tachycardia (VT), ventricular fibrillation (VF) and so forth – treat accordingly (see arrhythmia section)
  - b. Arrhythmias are most common cause of death post-MI

3. One to four days post-MI, patient develops sudden onset SOB with muffled heart sounds, jugular venous distention (JVD), and hypotension: free wall rupture (signs of tamponade)
  4. Within 10 days post-MI, patient develops new harsh systolic murmur at left lower sternal border (LLSB): ventricular septal defect (VSD) from rupture of interventricular septum
  5. Patient develops SOB, blowing systolic murmur radiating to apex: papillary muscle rupture leading to acute mitral regurgitation
  6. Days after MI, patient has chest pain with pericardial rub and some ECG changes: pericarditis (treat with ASA/NSAIDs)
  7. Weeks to months post-MI, patient develops fever with chest pain relieved by sitting forward: Dressler syndrome (autoimmune pericarditis, treat with ASA/NSAIDs)
  8. Patient with chest tightness several days after MI, ECG shows ST elevations: recurrent infarction (same territory or different territory); check CK-MB, since levels return to normal faster than troponin; send back to catheterization laboratory
- E. Miscellaneous**
1. Young woman with chest pain at night, ECG shows ST elevations: Prinzmetal angina (coronary vasospasm), diagnose with coronary angiography, treat with calcium channel blocker (CCB)
- F. Hints:** if initial troponin negative, recheck 6 to 8 hours later; do not need to know details of new anticoagulation/antiplatelet agents, do not need to memorize TIMI Risk Score

## II. Heart Failure

Think about left versus right heart failure symptoms, systolic versus diastolic categories, and the common causes tested on the shelf: coronary artery disease (CAD), hypertension (HTN), valvular heart disease, drugs/toxins (alcohol, cocaine, meth, anthracyclines), cardiomyopathies (discussed later), arrhythmias, lung disease, thyroid disease

### A. Symptoms/Signs

1. Right upper quadrant (RUQ) discomfort, peripheral edema, bloating: right-sided heart failure (hepatomegaly, JVD, hepatjugular reflux)
2. Dyspnea, orthopnea, paroxysmal nocturnal dyspnea (PND): left-sided heart failure (pulmonary edema with rales on examination)

**B. Diagnosis:** brain natriuretic peptide (BNP; falsely low in obese), ECG, chest x-ray (CXR), echocardiography

**C. Treatment of Acute Heart Failure:** *LMNOP* (Lasix, Morphine, Nitrates, Oxygen, Position)

1. Improve cardiac output by optimizing preload (e.g., reducing excessive preload with diuresis, salt/fluid restriction), afterload (e.g., ACE inhibitor, hydralazine, nitrates), and contractility (e.g., dobutamine, milrinone)

### D. Treatment of Chronic Heart Failure

1. Systolic dysfunction: heart failure with reduced ejection fraction (EF)
  - a. Treatment is based on stage of disease; however, know that these treatments improve mortality: ACEI (ARB second line if ACEI

not tolerated, hydralazine + nitrates third line or added for symptomatic improvement),  $\beta$ -blocker, spironolactone, cardiac resynchronization therapy (CRT), implantable cardiac defibrillator (ICD), omega-3 fatty acids

- b. These agents are helpful but do *not* decrease mortality: diuretics, digoxin
- c. Treatment for *every* patient: salt-restricted diet, fluid restriction, exercise, stop smoking or drinking alcohol
2. Diastolic dysfunction: heart failure with preserved EF
  - a. Impaired relaxation from MI, left ventricular hypertrophy (LVH; from HTN or other cause), hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy, hypothyroidism
  - b. No good treatments to decrease mortality; treat with diuretics, blood pressure (BP) control, and so forth
- E. **Hints:** always consider infection (e.g., pneumonia), dietary or medication noncompliance, MI, or arrhythmia (e.g., a-fib) as causes of an acute exacerbation; pulmonary artery catheterization (PAC) using Swan–Ganz catheter is controversial and usually not the right answer

### III. Arrhythmias

#### A. Atrial Fibrillation

1. Causes: HTN most common, CHF; other causes: **PIRATES** (Pulmonary disease, Ischemia, Rheumatic heart disease, Atherosclerosis/ Atrial myxoma, Thyrotoxicosis, Ethanol, Sepsis)
2. Treatment: depends on whether new onset or chronic, **CHADS<sub>2</sub>** score
  - a. If unstable, cardiovert
  - b. New onset but stable: rate control  $\rightarrow$  anticoagulate (heparin)  $\rightarrow$  cardiovert (if onset <48 hours), or first check transesophageal echo (TEE) or empiric anticoagulation  $\times$  3 weeks  $\rightarrow$  anticoagulation  $\times$  4 weeks after cardioversion
  - c. For chronic a-fib, rate control = rhythm control (therefore, can control the rate with  $\beta$ -blocker, CCB, digoxin); do not pick an antiarrhythmic for the answer choice
  - d. Anticoagulation for risk of embolic stroke based on **CHADS<sub>2</sub>**: 1 point for CHF, HTN, Age >75, diabetes mellitus (DM), and 2 points for previous Stroke/transient ischemic attack (TIA)
    - if 0 points, ASA; if 1 point, ASA or warfarin (goal INR 2 to 3); if  $\geq 2$  or valvular a-fib, warfarin
    - Note: the new oral anticoagulants such as rivaroxaban, dabigatran, apixaban, and so forth may be used alternatively but this is less likely to be tested
3. Hints: “irregular rhythm” or “irregularly irregular rhythm” on physical examination, almost always a-fib on the test; in patient with new onset a-fib, check TSH and electrolytes

#### B. Tachyarrhythmias: first, start with narrow or wide complex

1. Supraventricular tachycardia (narrow complex)
  - a. Atrial flutter: “sawtooth pattern” on ECG
  - b. Sinus tachycardia: causes include pain, fever, hypovolemia, hypoxemia, anemia, anxiety, venous thromboembolism, hyperthyroidism

- c. Multifocal atrial tachycardia (MAT), atrial tachycardia (AT), atrioventricular reciprocating tachycardia (AVRT), and AV nodal reentrant tachycardia (AVNRT) less commonly tested; most common rhythm in digoxin toxicity is atrial tachycardia with AV block
- d. Wolff–Parkinson–White (WPW): pre-excitation with delta waves on ECG, can cause re-entrant current → symptomatic tachycardia
  - Hints: do not give  $\beta$ -blocker or CCB if underlying disease (and not in AVRT); may precipitate AVRT due to slowing of conduction through the AV node
  - Give procainamide to rate control; ablation is usually successful
2. Ventricular tachycardia (wide complex): just be able to recognize on ECG; consider torsades de pointes with prolonged QT
  - a. For the shelf, answer will usually be to shock the patient (unless torsades, in which case you give magnesium)

### C. Bradyarrhythmias

1. AV block: first-degree (PR interval >200 ms), second-degree Mobitz I (Wenckebach, gradual prolongation of the PR interval until a beat is dropped), second-degree Mobitz II (occasional dropped beat without the Wenckebach pattern), third-degree (complete AV dissociation; P waves and QRS complexes fire at their own rates)
  - a. Mobitz II and third degree need pacemakers
2. Hints: make sure medications are not the cause ( $\beta$ -blocker, CCB, digoxin, antiarrhythmics, morphine); likely to show ECG on examination and identify the type of AV block

## IV. Valvular Disease

- A. **General Principles:** for most questions, treatment will be surgical replacement/repair if symptomatic
- B. **Aortic Stenosis (AS):** “midsystolic crescendo–decrescendo murmur at right upper sternal border (RUSB)” radiating to carotids, delayed carotid upstroke
  1. If young, bicuspid valve; if older, calcified valve
  2. Important symptoms: ASD (Angina, Syncope, Dyspnea of heart failure); predicts mortality, 5–3–2 years to live, respectively
  3. Managed surgically; replace valve when symptoms appear (do not memorize AS classification based on valve area, mean gradient, etc.)
  4. Hints: can cause acquired von Willebrand disease
- C. **Aortic Regurgitation (AR; also called aortic insufficiency):** “early diastolic decrescendo murmur at left upper sternal border (LUSB)”
  1. Causes: for shelf, think dilated aortic root or infective endocarditis
  2. Treatment is complicated; medical therapy with vasodilators or surgical valve replacement/repair
  3. Hints: always consider when you see a *wide pulse* pressure
- D. **Mitral Stenosis (MS):** “opening snap” with “low-pitched mid diastolic rumble at apex”
  1. Causes: think rheumatic heart disease (immigrant patient with lots of sore throats as a kid)

2. “*Tight is tight*” (closer opening snap to S2 = worse MS)
  3. Treatment: percutaneous mitral valvotomy, surgery, medical management with  $\beta$ -blockers and careful diuresis
  4. Hints: commonly causes a-fib from left atrial (LA) enlargement
- E. Mitral Regurgitation (MR):** high-pitched “holosystolic blowing murmur at the apex radiating to the axilla”
1. Causes: post-MI papillary muscle displacement/rupture or in the setting of mitral valve prolapse (MVP) from myxomatous degeneration, dilated cardiomyopathy
  2. Treatment: surgery for severe MR or symptoms, no medical management
- F. Mitral Valve Prolapse:** “midsystolic click” +/- late systolic murmur
- G. Tricuspid or Pulmonic Regurgitation:** think infective endocarditis in IV drug user
- H. Prosthetic Heart Valves:** anticoagulate the patient
- I. Hints:** only murmurs that get louder upon standing or with valsalva are HCM, MVP

## V. Cardiomyopathies

- A.** Not tested in detail, just know types and etiologies based on patient presentation
- B. Dilated Cardiomyopathy:** large, dilated heart with decreased contractility causing heart failure symptoms
1. High-yield causes: MI/CAD, valvular disease with volume overload (e.g., MR), infectious (TB, Chagas, HIV, coxsackie myocarditis sequelae, many others), drugs/toxins (anthracyclines, alcohol, cocaine), longstanding tachycardia, acromegaly, pheochromocytoma
    - a. Also, high-output heart failure: hypothyroidism, anemia, sepsis, arteriovenous fistulas, Paget disease, wet beriberi (thiamine deficiency)
- C. Restrictive Cardiomyopathy:** decreased ventricular compliance without pericardial disease
1. High-yield causes: amyloidosis (AL vs. AA), sarcoidosis, hemochromatosis, carcinoid, other autoimmune conditions (e.g., scleroderma)
- D. Hypertrophic Cardiomyopathy:** autosomal dominant, consider in young athlete with syncope and family history (FH) of sudden death; treat with  $\beta$ -blockers (some surgical procedures available, but unlikely to be tested)

## VI. Pericardial Disease

- A. Pericarditis:** consider in young patient with chest pain relieved by sitting forward, may see effusion; ECG shows diffuse ST elevation (concave up); commonly tested etiologies include viral (coxsackie, HIV), TB, uremia, Dressler syndrome, radiation
- B. Pericardial Tamponade:** can result from acute collection of fluid in pericardial space (CXR might show normal sized heart) or chronic collection of fluid (CXR will show “water bottle sign”)
1. Causes: malignancy, uremia, idiopathic, trauma, aortic dissection, ventricular free wall rupture (post-MI)

2. Clinical manifestations: *Beck triad* (distant heart sounds, JVD, hypotension), pulsus paradoxus, cardiogenic shock
  3. Look for echo showing effusion, septal shift with inspiration, diastolic collapse of right atrium (RA)/RV
  4. Treatment: always pericardiocentesis if unstable; can give fluids and inotropes
- C. Constrictive Pericarditis:** will look like right heart failure + thickened/calcified pericardium on CXR or CT; or just with clinical signs shown below
1. Signs: JVD, prominent x and y descents (of venous waveform), *Kussmaul sign*, pericardial knock, findings of right heart failure
  2. Causes: TB, postviral, uremia, radiation
  3. Treatment: diuresis if overloaded, pericardiectomy

## VII. Patient Presentations

- A. Chest Pain:** always consider multiple organ systems (cardiac, pulmonary, GI, etc.) but think cardiac first
1. Differential diagnosis (ddx)
    - a. Cardiac: ACS, peri-/myocarditis, aortic dissection
    - b. Pulmonary: pneumonia, pneumothorax, pulmonary embolism (PE)
    - c. GI: gastroesophageal reflux disease (GERD), diffuse esophageal spasm, peptic ulcer disease (PUD)
    - d. Others: musculoskeletal (MSK) conditions such as costochondritis, psychiatric diagnoses (e.g., panic disorder, anxiety)
- B. Syncope:** loss of consciousness (LOC) from cerebral hypoperfusion
1. LOC during emotional event with diaphoresis, “tunnel vision,” and ability to brace for the fall: vasovagal (neurocardiogenic syncope)
  2. Sudden LOC with no preceding symptoms, alert upon awakening, hit face on ground: cardiac etiology (e.g., arrhythmia, massive MI)
  3. Above, but during exercise: cardiac etiology (valvular disease, esp. AS; HCM)
  4. Aura, loss of continence, tongue biting, convulsions, confusion upon awakening: seizure (technically not “syncope,” but in the ddx)
  5. Elderly patient with LOC after standing up and feeling dizzy: orthostatic hypotension
  6. Sudden nervousness, heart pounding, sweating, feels like they will die: panic disorder

## VIII. Miscellaneous

- A. Aortic Dissection:** sharp, tearing chest pain radiating to back; type A (involving proximal aorta) requires immediate surgery, type B (descending aorta) managed with BP control
- B. Shock:** will need to recognize and diagnose the cause; specifics of treatment usually not tested
1. Types: hypovolemic (hemorrhage, diuresis or postdialysis, dissection, GI bleed), cardiogenic (MI, valvular disease, arrhythmia), distributive (sepsis, anaphylactic, neurogenic, meds, adrenal insufficiency), obstructive (PE, tension pneumothorax, tamponade)

Pulmonology

Pulmonary diseases are extremely high yield, both on the shelf examination (15% to 20% of questions) as well as Step 2 CK. Make sure you thoroughly understand obstructive lung diseases such as chronic obstructive pulmonary disease (COPD) – the clinical presentation, pathophysiology, diagnosis with pulmonary function tests, and treatment options (both chronically and for acute exacerbations). Restrictive lung diseases are slightly lower yield, but still important to recognize and diagnose.

- I. **Pulmonary Function Tests (PFTs):** *very high yield for the shelf, can differentiate restrictive from obstructive lung disease (Table 13-2)*  
If forced expiratory volume in 1 second (FEV<sub>1</sub>) responds to bronchodilators, then asthma; if no response, then COPD
  - A. **Diffusion Capacity of the Lung for Carbon Monoxide (DLCO):** evaluates functional surface area for gas exchange
    - 1. Obstructive: low in emphysema; restrictive: low in interstitial lung disease (ILD), CHF; normal spirometry: low in PE, vasculitis, anemia
    - 2. High in asthma, hemorrhage, polycythemia, pulmonary shunts (left → right)

- II. **Obstructive Lung Disease**
  - A. **COPD:** chronic airway and parenchymal inflammation (chronic bronchitis and emphysema)
    - 1. Diagnosis: see spirometry table above; look for symptoms/signs of dyspnea, chronic cough, barrel chest, hyper-resonance on percussion, distant lung and heart sounds, scattered expiratory wheezes, prolonged expiratory phase, decreased diaphragmatic excursion; technical diagnosis of emphysema is pathologic (based on biopsy), chronic bronchitis is clinical (productive cough >3 mo/y for ≥2 years)

Table 13-2 Pulmonary Function Testing

|                      | Obstructive | Restrictive         |
|----------------------|-------------|---------------------|
| <b>Spirometry</b>    |             |                     |
| FEV1                 | Low         | Normal/slightly low |
| FEV1/FVC             | Low         | Normal/high         |
| Peak expiratory flow | Low         | Normal              |
| <b>Volume</b>        |             |                     |
| Total lung capacity  | High        | Low                 |
| Vital capacity       | Low         | Low                 |
| Residual volume      | High        | Variable            |



- a. If old with extensive smoking history, think smoking as cause (centrilobular emphysema)
  - b. If young +/- liver disease, think  $\alpha_1$ -antitrypsin deficiency (panacinar emphysema) – shelf favorite
2. Treatment
    - a. Chronic disease: step-up therapy (do not need to memorize GOLD Staging Criteria and specifics; if patient is not doing well, add the next step therapy)
      - Start with bronchodilators: anticholinergic, short-acting  $\beta$  agonist (SABA), or both in combo
      - If inadequate response, add long-acting  $\beta$  agonist (LABA)
      - If inadequate response, add inhaled steroids
      - Additional options: theophylline, mucolytics, pulmonary rehabilitation, surgery (e.g., lung volume reduction), transplant
      - Influenza and pneumococcal vaccines, smoking cessation
    - b. COPD exacerbation: increased dyspnea, increased cough, and/or increased sputum production
      - First-line: ipratropium
      - Add:  $\beta_2$  agonist (albuterol), steroids (methylprednisolone IV or prednisone PO), antibiotics,  $O_2$ , low threshold for intubation
      - Oxygen: maintain  $SpO_2$  at 90% to 94% ( $PaO_2 > 60$  to 70) – if higher, will get  $CO_2$  retention (V/Q mismatch, Haldane effect, loss of hypoxic respiratory drive)
    - c. Shown to decrease mortality: *smoking cessation*, home  $O_2$  (if  $SpO_2 \leq 88\%$  or  $PaO_2 \leq 55$ )
  3. Complications: acute exacerbations, cor pulmonale, chronic hypercapnia (respiratory acidosis with compensatory metabolic alkalosis), polycythemia
  4. Hints: if new onset clubbing in COPD patient, think lung cancer
- B. Asthma:** chronic inflammation with airway hyper-responsiveness and variable airflow obstruction
1. Atopic triad: allergic rhinitis, atopic dermatitis (eczema), asthma
  2. For the most part, think of asthma similarly to COPD in diagnosis and treatment, with the following exceptions:
    - a. Chronic step-up treatment: SABA as a rescue medication  $\rightarrow$  +low-dose inhaled corticosteroids (ICS)  $\rightarrow$  +LABA  $\rightarrow$  +med/high-dose ICS (or leukotriene antagonist or theophylline)  $\rightarrow$  +oral steroids
    - b. Exacerbation: albuterol is first-line therapy (not ipratropium, but ipratropium can be adjunct),  $O_2$ , steroids, magnesium, intubation; *no antibiotics* (unless clear evidence of infection)

### III. Restrictive Lung Disease: know how to diagnose with PFTs and some of the relationships between the types of ILD

**A.** CHF, infections, and malignancy can mimic ILD

**B.** Important etiologies of ILD

1. African American patient with dyspnea and chronic cough, CXR shows bilateral hilar adenopathy, biopsy shows noncaseating granulomas: sarcoidosis, treat with corticosteroids

2. Elderly patient with chronic a-fib on rhythm control developing worsening dyspnea: iatrogenic (amiodarone); also consider radiation exposure (e.g., history of childhood lymphoma)
3. Patient with saddle nose deformity and hematuria: Wegener granulomatosis (granulomatosis with polyangiitis), c-ANCA (+)
  - a. Other collagen vascular diseases that cause ILD: scleroderma, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), other vasculitides (Churg–Strauss, microscopic polyangiitis), Goodpasture syndrome
4. If patient's occupation is given, and it is unusual, always consider environmental exposures (pneumoconioses)
  - a. Patient with lower-lobe fibrosis, calcified pleural plaques: asbestosis
    - Most common cancer in these patients is bronchogenic carcinoma, risk multiplied if smoker; most common cause of mesothelioma is asbestosis, but still rare
  - b. Patient with upper-lobe opacities and “eggshell calcifications” of lymph nodes: silicosis (mining, stone cutting, glass manufacturing); increased risk of TB (check PPD)
  - c. Patient with symptoms/signs of sarcoid (granulomas, skin lesions, hypercalcemia): berylliosis
  - d. Coal worker's pneumoconiosis (inhaled coal dust with carbon and silica)

#### IV. **Pulmonary Embolism:** understand the risk factors but will not directly test Wells criteria

- A. **Risk Factors (Virchow triad):** stasis (air travel), trauma/surgery (esp. ortho surgery), inherited hypercoagulable states, malignancy, or oral contraceptive pills (OCPs); previous deep venous thrombosis (DVT) or PE
- B. **Symptoms/Signs:** dyspnea, pleuritic chest pain, tachycardia, tachypnea, cough, hemoptysis, rales, cyanosis; also look for evidence of lower-extremity DVT (erythema, asymmetric leg swelling, palpable cord)
  1. If syncope, hemodynamic instability, and so forth, think massive PE (saddle embolus)
- C. **Workup:** CXR usually normal, ECG showing sinus tachycardia or right heart strain (S1Q3T3), arterial blood gas (ABG) showing hypoxemia with low CO<sub>2</sub> (respiratory alkalosis) and increased A–a gradient
  1. If high probability of PE, CT angiogram (V/Q scan if CT not available or contraindicated)
    - a. Renal failure is a contraindication (contrast is nephrotoxic)
  2. If low probability, D-dimer (high sensitivity; if negative, PE ruled out)
  3. Consider lower-extremity ultrasound to look for DVT
- D. **Treatment:** if high suspicion, start heparin (other agents, such as enoxaparin, work well too)
  1. If DVT found, same treatment as for PE (acute anticoagulation followed by chronic anticoagulation for 3 to 6 months)

2. If massive PE and hemodynamically unstable, may consider fibrinolytics or surgical/catheter thrombectomy
3. Inferior vena cava (IVC) filter in those with contraindication to anti-coagulation

**V. Pleural Effusion:** shelf questions primarily focus on differentiating transudate versus exudate (history will help!) as well as what the next step would be; low threshold for thoracentesis

- A. Transudate versus Exudate,** use *Light criteria* (exudate defined by at least one of the following): total effusion protein to total serum protein ratio  $>0.5$ , effusion LDH to serum LDH  $>0.6$ , or effusion LDH  $>$ two-thirds the normal upper limit of serum LDH
  1. Transudate: CHF, cirrhosis, nephrotic syndrome
  2. Exudate: infection (parapneumonic effusion), malignancy, PE, collagen vascular disease, GI disease (e.g., pancreatitis), hemothorax, chylothorax, Meigs syndrome (ovarian tumor)
- B. Complicated versus Uncomplicated** (parapneumonic effusion): complicated if pleural fluid gram stain or culture (+), pH  $<7.2$ , or glucose  $<60$
- C. Hints based on pleural fluid from thoracentesis**
  1. Low glucose: think rheumatoid arthritis (or malignancy, infection)
  2. High lymphocytes: TB
  3. Elevated amylase: pancreatitis or esophageal rupture
  4. High triglycerides: chylothorax
  5. Many RBCs: hemothorax, malignancy, PE
- D. Treatment:** if symptomatic, thoracentesis; complicated parapneumonic needs to be drained – tube thoracostomy or video-assisted thoracoscopic surgery (VATS) if loculated empyema; uncomplicated parapneumonic just needs antibiotics for pneumonia
  1. Note: if CHF, treat the CHF (no thoracentesis unless symptomatic)

**VI. Pneumothorax**

- A. Spontaneous:** consider in young patient with sudden onset of shortness of breath; cause is ruptured apical blebs; treatment is usually chest tube unless small and asymptomatic
- B. Tension:** decreased breath sounds on affected side, tracheal deviation away from affected side, mediastinal shift with hypotension and JVD; caused by creation of one-way valve; treatment is immediate needle thoracostomy in second intercostal space followed by chest tube placement (fifth intercostal space in midaxillary line)

**VII. Acute Respiratory Distress Syndrome (ARDS):** not heavily tested, just be able to recognize

- A. Definition:**  $\text{PaO}_2/\text{FiO}_2$  ratio  $<200$ , bilateral infiltrates on CXR, pulmonary capillary wedge pressure (PCWP)  $<18$  (noncardiogenic etiology)
  1. Note:  $\text{PaO}_2/\text{FiO}_2$  ratio of 200 to 300 is defined as acute lung injury (ALI)
- B. Causes:** pneumonia, sepsis, shock, trauma, aspiration, inhalation injury, diffuse intravascular coagulation (DIC), pancreatitis

- C. **Hints:** for treatment, the question may be a “next step” question, in which the answer is commonly to intubate (do not worry about detailed ventilation settings, but the goal is high PEEP and low tidal volume)

### VIII. Lung Cancer

- A. **Solitary Pulmonary Nodule on CXR:** first step is to look at old imaging, second step is to get CT; based on CT findings, either biopsy or repeat CT later (observation)
1. Benign (granuloma, hamartoma) versus malignant (bronchogenic carcinoma, metastatic); risk of malignancy if large and spiculated
- B. **Paraneoplastic Syndromes**
1. Small cell carcinoma: ADH (SIADH), ACTH (Cushing), Lambert-Eaton
  2. Squamous cell carcinoma: PTH-rp (hypercalcemia) – mnemonic: “*sCa<sup>2+</sup>mous*”
- C. **Other High-Yield Presentations**
1. Patient with face and arm erythema/swelling, distended neck veins and superficial chest wall veins, headache: superior vena cava (SVC) syndrome (central tumor compressing SVC)
  2. Patient with ptosis, miosis, anhidrosis, shoulder pain, atrophy of hand muscles: Pancoast syndrome (superior sulcus tumor) that can be impinging on the sympathetic chain (causing Horner syndrome) and on the brachial plexus
  3. Patient with hoarse voice (recurrent laryngeal nerve), dysphagia (esophageal compression), stridor (tracheal obstruction)

### IX. Patient Presentations

- A. **Dyspnea:** always start with cardiac versus pulmonary differential
1. Cardiac: CHF → pulmonary edema
  2. Pulmonary: obstructive (asthma, COPD, bronchiectasis), noncardiogenic pulmonary edema (ALI/ARDS), PE, pulmonary HTN, interstitial lung disease, hypoxemia (many causes)
- B. **Hemoptysis:** always consider lung cancer (older smoker), TB (immigrant or health care worker), PE (if risk factors), and vasculitis (Wegener granulomatosis, Goodpasture syndrome, Behçet disease); other causes include bronchitis (most common cause of trivial hemoptysis), bronchiectasis (esp. in cystic fibrosis)
1. Workup: differentiate pulmonary from GI bleed; if massive, then do angiography or rigid bronchoscopy to control the bleeding (shelf unlikely to ask specifics on workup and management)

## Nephrology

*Diseases of the genitourinary system make up 10% to 15% of shelf examination questions, with acute and chronic renal failure making up a large piece of that percentage. The most important parts of this section are knowing how to differentiate among the various causes of acute kidney injury, as well as knowing how to recognize chronic renal failure and its various complications.*

*Know the medications that act on the kidney (especially diuretics) and their side effects.*

- I. **Acute Kidney Injury (AKI):** abrupt increase in creatinine  $\geq 0.3$ , urine output (UOP)  $< 0.5$  cc/kg/h
  - A. **Prerenal:** think of anything causing decreased circulating volume (hypovolemia, CHF, sepsis, etc.) or renal vasoconstriction (NSAIDs, ACEI/ARB, hepatorenal syndrome); other causes include aortic dissection, renal artery stenosis (look especially for recent addition of ACEI to patient with unknown RAS)
    1. Diagnosis: fraction excretion of sodium (FENA)  $< 1\%$ , BUN/Cr  $> 15$
    2. Treatment: correct underlying disorder (give fluids, stop meds, etc.)
  - B. **Intrinsic:** look for FENA  $> 2\%$ , BUN/Cr  $< 15$ ; (FENA inaccurate with diuretics, check  $FE_{UREA}$  but this is unlikely to come up on shelf)
    1. Acute tubular necrosis (ATN): most common cause of AKI in hospital; can be caused by progression of prerenal AKI, from drugs (aminoglycosides, amphotericin, cisplatin), hemoglobin/myoglobin (crush injuries and rhabdomyolysis), light chains (multiple myeloma), crystals (acyclovir, methotrexate, indinavir), or contrast
      - a. Diagnosis: muddy brown casts on urinalysis (UA)
      - b. Treatment: watch out for post-ATN diuresis causing hypovolemia and worsening renal function (give plenty of fluids to make net ins = outs)
    2. Acute interstitial nephritis: causes include drugs ( $\beta$ -lactams, sulfa drugs, NSAIDs), pyelonephritis, *Legionella*; other causes uncommonly tested are sarcoid, lymphoma, SLE
      - a. Diagnosis: WBCs and WBC casts, urine eosinophils
    3. Other intrinsic causes: cholesterol emboli (patient after coronary angiogram, urine eosinophils), hemolytic uremic syndrome (HUS)/thrombotic thrombocytopenic purpura (TTP), DIC, glomerulonephritis
  - C. **Postrenal:** think obstruction, either bilateral ureters (nephrolithiasis, retroperitoneal mass/fibrosis) or bladder/urethra (bladder cancer, benign prostatic hyperplasia); high yield: anticholinergic meds in elderly patient
    1. Diagnosis: renal ultrasound
- II. **Chronic Renal Failure:** just know the basics (common causes and findings in uremia)
  - A. **Causes:** for shelf, always think HTN or DM first; others include glomerular disease, progression of AKI, polycystic kidney disease, multiple myeloma
  - B. **Complications (uremia):** encephalopathy, HTN, hyperlipidemia, CHF, anemia (low erythropoietin), bleeding, electrolyte abnormalities (hyperkalemia, hyperphosphatemia, hypocalcemia), osteodystrophy, pericarditis
  - C. **Indications for Dialysis:** **AEIOU** (Acidemia, Electrolytes, Ingestions, fluid Overload, Uremic encephalopathy/pericarditis/bleeding)

### III. Nephrotic Syndrome

- A. **Definition:** proteinuria ( $>3.5$  g/d) + edema + hypoalbuminemia + hypercholesterolemia
- B. **Types**
  1. Patient with nodular glomerulosclerosis: DM (Kimmelstiel–Wilson lesions)
  2. Patient with HIV: focal segmental glomerulosclerosis (FSGS)
  3. Patient with autoimmune disease (SLE, RA, etc.), non-Hodgkin lymphoma, hepatitis B virus (HBV)/hepatitis C virus (HCV), syphilis, or on NSAIDs: membranous; “spike and dome” pattern on light microscopy, subepithelial immune complex deposition on electron microscopy/immunofixation
  4. Patient with HCV, HIV, cryoglobulinemia or immune complex disease or C3 nephritic factor: membranoproliferative; “splitting” of capillary wall on light microscopy, subendothelial immune complex deposition on electron microscopy/immunofixation

### IV. Nephritic Syndrome: inflammatory process; proteinuria (not meeting definition of nephrotic syndrome) with hematuria (and RBC casts)

- A. Patient with hematuria a week after sore throat (or cellulitis): poststreptococcal glomerulonephritis
- B. Patient with hematuria, c-ANCA positive (Wegener granulomatosis), p-ANCA positive (microscopic polyangiitis), or Goodpasture syndrome (also with hemoptysis)
- C. Patient with hematuria after upper respiratory infection (URI): Berger disease (IgA nephropathy)

### V. Electrolytes

- A. **Hyponatremia:** ddx based on volume status
  1. Hypovolemic: “syndrome of appropriate ADH” (increased ADH is a physiologic response to low blood volume); also consider diuretics
  2. Euvolemic: SIADH (think of paraneoplastic syndrome, stroke, drugs), hypothyroidism, adrenal insufficiency
    - a. Also consider primary polydipsia (psych patient) or low solute intake (beer/tea and toast)
  3. Hypervolemic: CHF, cirrhosis, renal failure
  4. Treatment: if unstable (altered mental status, seizures, etc.) give hypertonic saline; otherwise, for the shelf, fluid restriction  $\pm$  diuretics (do not correct too fast or there is a risk of central pontine myelinolysis)
  5. Hints: beware pseudohyponatremia (hyperproteinemia, hyperlipidemia) or hyperosmotic hyponatremia (hyperglycemia, hypertonic infusions such as mannitol)
- B. **Hypernatremia:** can be caused by renal, GI, or insensible water losses as well as sodium overload; diabetes insipidus (DI) is most tested cause, which will present with severe polyuria, polydipsia, with mild hypernatremia (as long as patient can keep drinking water to replace losses)
  1. Central DI: ADH not being released; causes include trauma/surgery to hypothalamus/pituitary, tumor, Sheehan syndrome

- a. Diagnosis: responds to exogenous ADH (urine osmolality increases)
  - b. Treatment: exogenous DDAVP
- 2. Nephrogenic DI: ADH having no effect on kidneys; common causes on the shelf include meds (lithium, demeclocycline, amphotericin), ATN with postobstruction diuresis, electrolyte disturbance (hypercalcemia, hypokalemia), sickle cell anemia
  - a. Diagnosis: no response to exogenous ADH (urine osmolality unchanged)
  - b. Treatment: low sodium diet, thiazide diuretics
- 3. Treat hyponatremia by replacing free water (e.g., D5 W, ½NS) but do not correct too fast or else cerebral edema (leading to brainstem herniation)
- C. **Hyperkalemia:** causes include acidemia, end-stage renal disease (ESRD), massive cellular necrosis (e.g., tumor lysis syndrome, rhabdomyolysis, hemolysis), meds ( $\beta$ -blockers, succinylcholine)
  - 1. Look for peaked T waves, prolonged PR and QRS duration, sinusoidal pattern (late)
  - 2. Treat immediately with calcium to stabilize cardiac membrane; insulin + glucose will shift potassium intracellularly; other options are sodium bicarbonate, kayexalate (sodium polystyrene), albuterol; dialysis always an option if previous methods fail
- D. **Hypokalemia:** causes include GI losses (vomiting, diarrhea), alkalemia, renal losses (diuretics, diabetic ketoacidosis, renal tubular acidosis, Bartter syndrome/Gitelman syndrome), magnesium depletion, hyperaldosteronism
  - 1. Look for U waves and increased QT interval on ECG
- E. **Hypercalcemia:** for shelf, think of hyperparathyroidism, Paget disease, cancer, excess supplements (calcium or vitamin D), sarcoidosis
  - 1. Look for “stones, bones, groans, psychiatric overtones” and shortened QT interval
- F. **Hypocalcemia:** for shelf, think of hypoparathyroidism, ESRD, low vitamin D
  - 1. Look for Chvostek sign, Trousseau sign, prolonged QT interval
  - 2. Hints: look out for falsely low calcium in the setting of low albumin (total calcium lower, but free, ionized calcium normal)

## VI. Acid/Base: not complicated on the shelf, usually just a primary disorder with compensatory response

- A. **Approach:** check pH, then  $\text{HCO}_3^-$  and  $\text{PaCO}_2$  (Table 13-3)
- B. Always look for an anion gap [ $\text{Na} - (\text{Cl} + \text{HCO}_3^-)$ ] >12; gap = metabolic acidosis
  - 1. Mnemonic is **MUDPILERS**: Methanol, Uremia, Diabetic ketoacidosis (DKA), Paraldehyde, Isoniazid (INH)/Iron, Lactic acidosis, Ethylene glycol/EtOH ketoacidosis, Rhabdomyolysis, Salicylates/Starvation ketoacidosis
  - 2. Beware hidden gap with low albumin (corrected gap = calculated gap + 2.5 for each drop in albumin by 1; e.g., if calculated gap is 10 and albumin is 2, then actual gap is 15)

**Table 13-3 Acid/Base Overview**

|                       | $\text{PaCO}_2$ | $\text{HCO}_3$ |
|-----------------------|-----------------|----------------|
| Metabolic acidosis    | ↓               | ↓              |
| Metabolic alkalosis   | ↑               | ↑              |
| Respiratory acidosis  | ↑               | ↑              |
| Respiratory alkalosis | ↓               | ↓              |

- C. Nonanion gap metabolic acidosis
  - 1. Mnemonic is **HARDPUT**: Hyperalimentation, Acetazolamide, Renal tubular acidosis (RTA)/Renal failure, Diarrhea, Pancreatic fistula, Ureteral diversion, Toluene
- D. **Metabolic Alkalosis**: on shelf, consider vomiting, diuretics, mineralocorticoid excess, severe hypokalemia
- E. **Respiratory Acidosis**: hypoventilation, COPD, pleural effusions, pneumothorax, pulmonary edema
- F. **Respiratory Alkalosis**: compensatory response to metabolic acidosis, respiratory distress, salicylates, pregnancy, anxiety, PE
- G. Consider checking for compensatory response to primary insult (e.g., compensatory respiratory alkalosis for a metabolic acidosis)
- H. **High Yield**: ASA overdose causes primary metabolic acidosis and primary respiratory alkalosis

## VII. **Nephrolithiasis**: presents as hematuria with flank pain radiating to the groin

### A. **Types of Stones**

- 1. Patient with abdominal pain, altered mental status, bone lesions: calcium stones (in setting of primary hyperparathyroidism)
  - a. Calcium stones are the most common type; can be calcium phosphate or calcium oxalate (look for calcium oxalate in Crohn disease)
  - b. Furosemide makes worse, thiazide helps
- 2. Patient with occasional severe pain of first metatarsal joint: uric acid stones (in setting of gout)
  - a. Stones are *radiolucent* on x-ray
- 3. Patient with recurrent urinary tract infections (UTIs), *Proteus* isolated from last urine culture: struvite stones (ammonium magnesium phosphate)
  - a. Caused by urease-positive organisms (*Proteus*, *Enterobacter*, *Klebsiella*) causing alkalized urine
- 4. Young patient with recurrent stones, examination shows hexagon-shaped crystals: cystine stones (in setting of cystinuria, an autosomal recessive disease)

### B. **Workup**: CT scan without contrast



- C. **Prevention:** increase fluid intake; if calcium stones, decrease sodium and meat intake, give thiazide diuretic, *increase* dietary calcium intake (decreases oxalate reabsorption in GI tract); if uric acid stones, alkalinize the urine, give allopurinol; if struvite, give antibiotics; if cystine stones, alkalinize urine

## VIII. Patient Presentations

### A. Hints for Evaluating UA

1. 3+ blood on dipstick but no RBCs on microscopy: myoglobinuria, think rhabdomyolysis
2. Dysmorphic RBCs or RBC casts: glomerular pathology (consider nephritic syndromes)
3. Muddy brown casts: ATN
4. WBC casts: pyelonephritis, acute interstitial nephritis, glomerulonephritis
5. Elevated WBCs, (+) leukocyte esterase, (+) nitrites: UTI
6. Urine eosinophils: acute interstitial nephritis
7. Homeless patient with altered mental status, serum osmolar gap and calcium oxalate crystals in urine: ethylene glycol intoxication

### B. Lower Urinary Tract Symptoms

1. Older patient with difficulty initiating stream, frequency, urgency, nocturia, diffusely enlarged prostate on examination: benign prostatic hyperplasia (BPH)
2. Same, but now with asymmetry or a nodule on prostate examination with low back pain: metastatic prostate cancer
3. Young patient with dysuria, urethral discharge, and so forth, and no systemic symptoms: sexually transmitted infection (STI)
4. Patient with dysuria, vision changes, polyarthritis: reactive arthritis ("can't see, can't pee, can't climb a tree")

- C. **Hematuria:** in older patients, always rule out renal cell carcinoma or bladder cancer with CT scan and cystoscopy; also think of nephritic syndromes; always consider meds (cyclophosphamide, rifampin)

- D. **Proteinuria:** consider in diabetic nephropathy; see if patient meets criteria for nephrotic syndrome

## Gastroenterology

*This is a large and cumbersome section, given that there are so many GI diseases with complicated management algorithms. It is important to know that many of these diseases make up a large part of the Surgery shelf examination (appendicitis, acute cholecystitis, etc.), but many are still high yield for the Medicine shelf examination. We have highlighted some of the more common topics that appear on the shelf, with specific advice on how to approach common GI complaints such as abdominal pain and patterns of abnormal liver function tests (LFTs).*

### I. Esophageal Disease

- A. **Achalasia:** spastic lower esophageal sphincter (LES), abnormal peristalsis

1. Dysphagia for both liquids and solids (hint: if solids only, mechanical obstruction such as tumor; if solids and liquids, motility disorder such as achalasia)
2. “Bird’s beak” on barium swallow; manometry confirms diagnosis; consider Chagas disease if patient has epidemiologic risk factors
3. Treatment: LES botox injection, dilation, surgery; nitrates and CCBs are only temporizing

## B. Esophageal Cancer

1. Dysphagia for solids > liquids, poor prognosis
  2. Adenocarcinoma: distal one-third of esophagus, risk factors are GERD and Barrett esophagus (columnar metaplasia of squamous epithelium, caused by longstanding GERD; high-yield risk factor for adenocarcinoma)
  3. Squamous cell carcinoma: upper and middle esophagus, risk factors are alcohol and tobacco use, HPV, achalasia
- C. **Diffuse Esophageal Spasm:** noncardiac chest pain, “corkscrew esophagus” on barium swallow; manometry is diagnostic
- D. **Zenker Diverticulum:** presents as dysphagia, regurgitation of undigested food, halitosis; caused by increased intraluminal pressure (cricopharyngeal spasm) leads to outpouching of mucosa above cricopharyngeus (pharyngoesophageal junction)
- E. **Esophageal Webs:** can be due to Plummer–Vinson syndrome (associated with iron-deficiency anemia, koilonychia, atrophic oral mucosa), sliding hiatal hernia, toxic ingestion

## II. Peptic Ulcer Disease (PUD)

- A. **Symptoms:** aching/gnawing epigastric pain, may radiate to back
- B. **Duodenal Ulcers:** eating relieves pain (therefore weight gain)
1. Caused by offensive factors: *H. pylori*, hypersecretion (e.g., gastrinoma), NSAIDs (including ASA)
    - a. **Hint:** if many duodenal ulcers, or if jejunal ulcers present, always consider Zollinger–Ellison syndrome (ZES, a gastrinoma); if high gastrin, can perform secretin stimulation test; consider MEN1
- C. **Gastric Ulcers:** pain worsened by eating (therefore weight loss); more commonly associated with malignancy
1. Caused by decrease in defensive factors; important causes include NSAIDs, *H. pylori*, smoking, stress (“Cushing ulcer” if CNS process, “Curling ulcer” if burn)
- D. **Workup**
1. Endoscopy is most accurate; can also use barium swallow
  2. *H. pylori*: biopsy (gold standard), urea breath test, serology (*not* used to confirm eradication), stool antigen (used to confirm eradication)
  3. Serum gastrin level
- E. **Treatment**
1. If *H. pylori* (+), start triple therapy: proton pump inhibitor (PPI), amoxicillin, clarithromycin
  2. Lifestyle (stop smoking and EtOH), stop NSAID if possible

3. Cytoprotection with sucralfate, misoprostol (particularly if patient requires NSAID)
4. Acid suppression: PPIs > H<sub>2</sub> blockers > antacids
- F. **Complications:** perforation, gastric outlet obstruction, upper GI bleed (most common cause)
- G. Gastritis may present similarly, can be acute or chronic, and has many of the same causes as PUD (NSAIDs, *H. pylori*, etc.)
  1. High yield: autoimmune gastritis leading to pernicious anemia (antibodies against parietal cells → loss of parietal cells → loss of intrinsic factor → B<sub>12</sub> malabsorption)

### III. Mesenteric Ischemia

#### A. Acute

1. Symptoms/signs: abdominal pain out of proportion to examination, nausea/vomiting, GI bleed, lactic acidosis
2. Causes: arterial embolism (acute onset, usually cardiac origin), arterial thrombosis (gradual onset), nonocclusive ischemia (vasoconstriction secondary to low cardiac output), venous thrombosis (treat with anticoagulation)

- B. **Chronic:** history of atherosclerosis, postprandial abdominal pain, weight loss

### IV. Inflammatory Bowel Disease (IBD): summarized in Table 13-4

#### V. Diverticular Disease

- A. **Etiology:** high intraluminal pressure (chronic constipation)
- B. Most common location is sigmoid colon; look for few, large, and right-sided (ascending colon) diverticuli in Asian population
- C. **Complications**
1. Painless hematochezia (common cause of lower GI bleed)
  2. Diverticulitis: due to obstruction of diverticulum with secondary bacterial overgrowth
    - a. Diagnose with CT scan with PO/IV contrast
    - b. Treat uncomplicated with IV antibiotics, bowel rest, IV fluids (IVF); treat complicated (abscess, colovesical fistula, obstruction, perforation) with surgery

### VI. Hepatobiliary Disease

- A. **Cirrhosis:** a diagnosis made by pathology; end-stage liver disease as evidenced by hepatocellular necrosis with bridging fibrosis
1. Causes: alcoholic, infectious hepatitis, drug toxicity (acetaminophen), autoimmune hepatitis, primary biliary cirrhosis (PBC), metabolic (hemochromatosis, Wilson disease), hepatic congestion,  $\alpha_1$ -antitrypsin
  2. Clinical features
    - a. Portal hypertension: ascites and varices (esophageal, hemorrhoids, caput medusae)
      - Treatment of variceal bleeds: esophageal/gastric bleeding has a high mortality rate, treat first by stabilizing hemodynamics,

**Table 13-4 Comparison of Crohn Disease and Ulcerative Colitis**

|               | Crohn Disease                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Ulcerative Colitis                                                                                                                         |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| Location      | <ul style="list-style-type: none"><li>• Can affect any part of GI tract, from mouth to anus; most commonly terminal ileum</li><li>• Skip lesions</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <ul style="list-style-type: none"><li>• Colon (distal to proximal) +/- "backwash ileitis"</li><li>• No skip lesions (continuous)</li></ul> |
| Pathology     | <ul style="list-style-type: none"><li>• Transmural (therefore can lead to fistulae) inflammation</li><li>• Noncaseating granulomas</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <ul style="list-style-type: none"><li>• Mucosal inflammation</li><li>• Crypt abscesses</li></ul>                                           |
| Complications | <ul style="list-style-type: none"><li>• Anorectal disease (fistulae in ano), SBO, nephrolithiasis (calcium oxalate stones), B<sub>12</sub> deficiency and steatorrhea (if ileum affected), gallstones, malabsorption</li><li>• Both: iron-deficiency anemia, malignancy (higher rate of colorectal cancer in UC)</li><li>• Extraintestinal manifestations: IBD-associated arthritis, uveitis, sacroiliitis, skin changes (erythema nodosum, pyoderma gangrenosum), thromboembolism</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                            | <ul style="list-style-type: none"><li>• Toxic megacolon, primary sclerosing cholangitis (less common in Crohn's), strictures</li></ul>     |
| Treatment     | <ul style="list-style-type: none"><li>• There is debate over appropriate initial treatment (bottom up or top down approaches); however, just know the treatment options and the potency of the agents so that treatment can be escalated if the disease worsens</li><li>• Steroids for induction and acute exacerbations</li><li>• Sulfasalazines (mesalamine, 5-ASA) for maintenance</li><li>• Immunosuppressants (azathioprine, 6-mercaptopurine)</li><li>• Metronidazole and/or ciprofloxacin for infectious complications; may be primary treatment if sulfasalazines fail in Crohn disease</li><li>• Colectomy is curative in UC (severe disease unresponsive to medical therapy, toxic megacolon, obstruction, perforation, prophyllaxis)</li><li>• Note: smoking increases the risk of Crohn's as well as recurrence; smoking may decrease the risk of UC (but still, do not encourage them to smoke!)</li></ul> |                                                                                                                                            |

emergent endoscopy when stable; IV octreotide, IV antibiotics for prophylaxis;  $\beta$ -blockers are long-term medical therapy; can also ligate/band, sclerotherapy, balloon tamponade; transjugular intrahepatic portosystemic shunt (TIPS) can also be used to form a shunt to decrease portal vein pressures

- Ascites: serum-ascites albumin gradient (SAAG) >1.1 suggests portal HTN; treat with spironolactone/furosemide

- Feared complication: spontaneous bacterial peritonitis, which presents with fever, abdominal pain, leukocytosis; perform paracentesis to diagnose and treat with ceftriaxone
  - b. Increased estrogen: spider angiomas (upper chest, blanch with pressure), palmar erythema; gynecomastia and testicular atrophy in males
  - c. Loss of hepatic synthetic function: coagulopathy – treat with fresh frozen plasma (FFP) if necessary; edema from loss of albumin
  - d. Elevated bilirubin: jaundice, light stools, dark urine
  - e. Hepatic encephalopathy: altered mental status with asterixis on examination; treat with lactulose, neomycin
  - f. Hypoglycemia
  - g. Hepatorenal syndrome: splanchnic dilatation with renal hypoperfusion
- B. Cholelithiasis:** more likely to see on the surgery shelf, but below is a quick review
1. Many are asymptomatic, but if symptomatic will present as RUQ/epigastric pain after fatty meals
  2. Types of gallstones
    - a. Cholesterol: obesity, diabetes, hyperlipidemia, OCPs, Crohn disease
    - b. Pigmented: hemolysis and alcoholic cirrhosis (black); infection (brown)
    - c. Mixed: majority of stones
  3. Treat recurrent biliary colic with elective cholecystectomy
  4. Complications
    - a. Acute cholecystitis: RUQ tenderness, (+) Murphy sign, ultrasound showing gallstones, thickened gallbladder wall, and pericholecystic fluid; can also use HIDA scan
      - Treatment: IV fluids and antibiotics, NPO, cholecystectomy after ~48 hours; percutaneous cholecystostomy is an alternative treatment for critically ill patients who cannot undergo cholecystectomy
      - Note: acalculous cholecystitis occurs in severely ill patients (ICU patients), caused by stasis (dysmotility) and not gallstones
    - b. Cholelithiasis: gallstones in common bile duct, can lead to stasis and cholangitis; ERCP is the gold standard
    - c. Cholangitis: infection of biliary tract secondary to obstruction
      - *Charcot triad*: RUQ pain, jaundice, fever; *Reynolds pentad*: Charcot triad + hypotension, confusion
      - Management: ultrasound and ERCP for diagnosis, IV fluids, and antibiotics
- C. Primary Sclerosing Cholangitis (PSC):** associated with ulcerative colitis; presents with cholestatic findings, can lead to liver failure or cholangiocarcinoma; ERCP shows “string of beads”
1. Treatment: symptomatic (cholestyramine for pruritus, stenting)
- D. Primary Biliary Cirrhosis (PBC):** autoimmune disease associated with antimitochondrial antibodies, most commonly seen in middle-aged women

1. Treatment: symptomatic, ursodeoxycholic acid slows progression; liver transplant
- E. **Wilson Disease:** autosomal recessive disease that presents with evidence of liver disease and neuropsychiatric symptoms/signs; look for Kayser-Fleischer rings on examination, diagnose with low ceruloplasmin and low serum copper; urine copper will be high

## VII. Pancreatitis

- A. **Etiologies** – *GET SMASHED*: Gallstones, EtOH abuse, Trauma, Steroids, Mumps and other viral infections, Autoimmune, Scorpion bites, Hypertriglyceridemia/Hypercalcemia, ERCP, Drugs (sulfonamides, thiazides, furosemides, estrogens, HIV meds)
- B. **Symptoms/Signs**
  1. Epigastric pain radiating to back, worse after meals
  2. Weight loss, diabetes, and steatorrhea indicate chronic pancreatitis
  3. Lipase is more specific than amylase for acute (normal in chronic)
  4. CT abdomen is most specific imaging for acute; pancreatic calcifications seen with chronic (can see on plain radiograph)
- C. **Complications**
  1. Sepsis, ARDS, ascites, pleural effusion
  2. Hemorrhagic pancreatitis: Grey Turner sign (flank ecchymosis), Cullen sign (periumbilical ecchymosis), Fox sign (inguinal ligament ecchymosis)
  3. Pancreatic necrosis: CT-guided aspiration and gram stain/culture, then debridement if infected
  4. Pancreatic pseudocyst: appears 2 to 3 weeks after acute attack; can cause infection, rupture, obstruction of abdominal viscera; differentiate from pancreatic abscess (4 to 6 weeks)
- D. **Treatment**
  1. Bowel rest with nasogastric tube (some say nasojejunal tube to bypass pancreas), IVF, pain control
  2. For chronic pancreatitis: pain control

## VIII. Malignancies

- A. **Gastric Cancer:** most are adenocarcinomas, others are lymphomas (non-Hodgkin lymphoma); risk factors include *H. pylori*, chronic inflammation (e.g., gastritis/PUD), nitrosamine foods
  1. Other facts: metastasis to ovaries called Krukenberg tumor; Virchow node is supraclavicular, Sister Mary Joseph node is periumbilical
- B. **Pancreatic Cancer:** most commonly presents with weight loss and vague abdominal symptoms; risk factors include smoking and chronic pancreatitis; mostly occur in head of pancreas, which may produce obstructive symptoms (jaundice, acholic stools); very poor prognosis
  1. Enlarged, nontender gallbladder (Courvoisier sign) and migratory thrombophlebitis (Trousseau sign) should raise concern
- C. **Colorectal cancer**
  1. Familial syndromes: familial adenomatous polyposis (FAP), hereditary nonpolyposis colon cancer (HNPCC), Gardners (polyps, osteomas, dental abnormalities, soft tissue tumors, sebaceous cysts),

Turcot syndrome (polyps, brain tumor), Peutz–Jeghers (GI tract hamartomas, intussusception)

2. Polyps
  - a. Appearance: sessile (flat) has greater risk of malignancy, pedunculated lower risk
  - b. Histology: tubular is most common and has least risk of malignancy, villous has greatest risk; tubulovillous has intermediate risk
3. Common presentation: older male with microcytic anemia; most common cause of colonic obstruction in adults; right-sided tumors tend to cause melena and iron-deficiency anemia, left-sided tumors tend to cause obstruction (thin stools) and hematochezia

## IX. Patient Presentations

**A. Dysphagia:** barium swallow then endoscopy; manometry for achalasia, 24-hour pH monitor for GERD; remember HIV status (can treat for Candida esophagitis empirically, but also consider CMV and HSV)

### B. GI Bleed

1. Ligament of Treitz is the boundary between upper and lower GI
2. Upper GI bleed causes: PUD (most common), reflux esophagitis, esophageal/gastric varices, gastric erosions, Mallory–Weiss tears, hemobilia, Dieulafoy malformation (submucosal dilated arterial), aortoenteric fistula after vascular surgery, neoplasm
3. Lower GI bleed causes: diverticulosis, angiodysplasia, IBD, cancer, ischemia, hemorrhoids, fissures
4. Extremely elevated BUN:creatinine ratio can suggest an upper GI bleed
5. Treatment: *hemodynamic support*; once stable, endoscopy and coagulation of bleeding vessel for upper GI bleed, and colonoscopy for lower GI bleed; surgery as last resort or if visible vessel at base of an ulcer

### C. Jaundice

1. Conjugated hyperbilirubinemia: dark urine, pale stools
  - a. Decreased excretion (intrahepatic): Dubin–Johnson syndrome, Rotor syndrome, PBC, PSC, hepatocellular disease; biliary obstruction (extrahepatic); gallstones, pancreatic carcinoma, cholangiocarcinoma, biliary atresia
2. Unconjugated hyperbilirubinemia
  - a. Excess production: hemolysis
  - b. Impaired conjugation or reduce uptake in the liver: Gilbert syndrome, Crigler–Najjar syndrome, diffuse liver disease

### D. Approach to LFTs

1. Cholestatic: markedly elevated alkaline phosphatase and GGT; moderately elevated AST/ALT
2. Hepatocellular: markedly elevated ALT/AST; normal or moderately elevated alkaline phosphatase
3. ALT/AST (transaminases)
  - a. If >10,000 think shock liver (ischemic hepatitis) or acetaminophen toxicity
  - b. High hundreds/thousands think acute viral hepatitis

- c. Low hundreds think chronic viral or acute alcoholic hepatitis
- d. AST:ALT >2:1 think alcoholic hepatitis
- 4. Alkaline phosphatase
  - a. Not specific for liver; if elevated, confirm hepatic source by elevated GGT (if GGT normal, then elevated alkaline phosphatase is due to bone disease or pregnancy)
    - Patient with high alkaline phosphatase, normal GGT, normal calcium: Paget disease
- 5. Tests of liver function: coagulation (PT/INR), albumin, bilirubin

Endocrine and Metabolic Disorders

*This section comprises an average of about 5% to 10% of shelf examination questions. Always consider whether the abnormality is primary (involving the gland itself) or secondary (caused by an upstream process). Because diabetes mellitus is so common in the United States, it is very important to know how to recognize and manage both the chronic manifestations as well as the acute complications (e.g., diabetic ketoacidosis).*

- I. **Panhypopituitarism:** know etiologies, and be able to recognize symptoms/signs of multiple hormone deficiencies (detailed individually below)
  - A. Important etiologies include surgery/trauma, ischemia (Sheehan syndrome if recent delivery), infection, gland infiltration (sarcoid, hemochromatosis), tumors (hypothalamis/pituitary, craniopharyngioma), radiation
  - B. Typically in hypopituitarism, the order of hormones lost are (1) FSH/LH, (2) GH, (3) TSH, (4) ACTH
    - 1. **Hint:** a trick to remember the order is by importance for immediate survival (sex < growth < metabolism < blood pressure)

II. Thyroid and Parathyroid Disease

- A. Diagnostic approach to thyroid disorders based on laboratory results (Table 13-5)

Table 13-5 Approach to Thyroid Disorders

|                                     | TSH       | T4        |
|-------------------------------------|-----------|-----------|
| Primary hyperthyroidism             | Decreased | Increased |
| Secondary (Central) hyperthyroidism | Increased | Increased |
| Subclinical hyperthyroidism         | Decreased | Normal    |
| Primary hypothyroidism              | Increased | Decreased |
| Secondary (Central) hypothyroidism  | Decreased | Decreased |
| Subclinical hypothyroidism          | Decreased | Normal    |



**B. Hyperthyroidism:** symptoms include weight loss, psychosis, anxiety, palpitations (common cause of a-fib), tremor, heat intolerance, hair loss, diarrhea

1. Graves disease: most common cause of hyperthyroidism, caused by antibodies that activate the TSH receptor; presents with diffusely enlarged thyroid +/- proptosis (Graves ophthalmopathy), erythema nodosum
  - a. Treatment: methimazole (high rate of recurrence, risk of agranulocytosis), propylthiouracil (PTU; second line, risk of hepatocellular necrosis), radioactive iodine (RAI; most become hypothyroid after), surgery (if obstructive goiter or ophthalmopathy); prednisone can be given for ophthalmopathy,  $\beta$ -blockers for symptoms
2. Toxic multinodular goiter: hyperfunctioning nodules, atrophic in other areas
  - a. Treatment of toxic multinodular goiter and toxic adenoma: RAI or surgery
3. Toxic adenoma: single, hyperfunctioning nodule
4. Hashimoto thyroiditis and subacute thyroiditis can cause transient hyperthyroidism; subacute is exquisitely tender, diffusely enlarged
5. Thyroid storm: life-threatening, treat with supportive therapy, antithyroid agents (propylthiouracil), iopanoic acid or iodide (inhibits thyroid hormone release),  $\beta$ -blockers, dexamethasone (inhibits T4  $\rightarrow$  T3 conversion)

**C. Hypothyroidism:** symptoms typically opposite of hyperthyroidism and include weight gain, fatigue, psychosis, cold intolerance, constipation; treatment is thyroid hormone replacement (levothyroxine)

1. Hashimoto disease: most common cause, rubbery nontender goiter; antithyroid peroxidase (anti-TPO) or antithyroglobulin (anti-Tg) antibodies
2. Subacute thyroiditis (after transient hyperthyroid state): occurs after viral infection, tender (sometimes asymmetric) gland
3. Fibrous thyroiditis (Riedel thyroiditis): patients may be hypothyroid or euthyroid
4. Iatrogenic: radioiodine, thyroidectomy, meds (lithium is high yield, look for bipolar patient with symptoms of hypothyroidism); also, look for patient taking levothyroxine with food or antacids (need to take on empty stomach to increase absorption)
5. Central (secondary, tertiary) hypothyroidism is rare, and is characterized by low levels of TSH as well as T3/T4

**D. Thyroid Cancer** (Table 13-6)

**E. Hyperparathyroidism**

1. Primary: usually caused by adenoma, as opposed to hyperplasia or carcinoma; the most common cause of hyperparathyroidism in outpatient setting
  - a. Symptoms/signs: "stones, bones, groans, psychiatric overtones"
    - Bones: aches, osteitis fibrosa cystica predisposing to pathologic fractures
    - Stones: nephrolithiasis

**Table 13-6 Summary of Thyroid Cancer Types**

|                | Papillary                                          | Follicular                                                                 | Medullary                                                                                                                     | Anaplastic                                         |
|----------------|----------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| Back-ground    | Most common type, least aggressive                 | Vascular/capsular invasion hallmark, Hürthle cell carcinoma a variant      | Associated with MEN II, arises from parafollicular (C) cells (others arise from follicular cells), calcitonin is tumor marker | Most rare, extremely malignant                     |
| Invasion       | Lymphatic spread                                   | Hematogenous spread                                                        | Lymphatic spread                                                                                                              | Lymphatic and hematogenous spread                  |
| Histopathology | Nuclear grooves, pseudoinclusions, psammoma bodies | Variable with follicles and colloid; difficult to distinguish from adenoma | Amyloid                                                                                                                       | Undifferentiated, does not resemble thyroid tissue |
| Prognosis      | Good                                               | Fair                                                                       | Fair                                                                                                                          | Poor                                               |

- Groans: abdominal pain, constipation, muscle pain, peptic ulcers, gout, pancreatitis
  - Psychic moans: depression, fatigue, anxiety
  - Others: polydipsia, polyuria, shortened QT interval
- b. Laboratory results: hypercalcemia (correct if low albumin), hypophosphatemia, hypercalciuria, inappropriately normal or high PTH
- c. Treatment: surgical resection
- Hyperplasia: resect all four glands (put some parathyroid tissue in forearm)
  - Adenoma: resect adenoma
  - Carcinoma: resect tumor, ipsilateral thyroid, lymph nodes
  - Fluids and loop diuretics (*not* thiazides) for severe hypercalcemia
2. Secondary: elevation in PTH secondary to low calcium, most commonly from chronic renal failure
3. Tertiary: after longstanding secondary hyperparathyroidism, autonomous PTH production; prevent with dietary changes and cinacalcet

**F. Hypoparathyroidism**

1. Usually occurs in the setting of recent head and neck surgery
2. Symptoms/signs are a result of hypocalcemia: tetany (Chvostek sign, Trousseau sign), prolonged QT, cardiac arrhythmias, circumoral numbness/paresthesia, rickets, osteomalacia

3. Laboratory results: low calcium, high phosphate, low PTH
4. Treatment: calcium supplementation (IV calcium for severe cases), vitamin D

### III. Adrenal Gland Disease

#### A. Hypercortisolism (Cushing Syndrome)

1. Symptoms/signs: “Cushingoid appearance” (central obesity, hirsutism, moon facies, dorsal fat pad “buffalo hump,” striae, acne, bruising), hypertension, decreased glucose tolerance, hypogonadism, proximal muscle wasting, osteoporosis, depression, mania
2. Causes
  - a. Primary: adrenal adenoma/carcinoma
  - b. Secondary: ACTH-secreting pituitary adenoma (Cushing disease) or ectopic ACTH production (small cell lung cancer)
  - c. Iatrogenic: most common, no androgen excess
3. Diagnosis
  - a. Screening after clinical suspicion: 24-hour urine cortisol or overnight dexamethasone suppression test
  - b. Overnight dexamethasone suppression test
    - If low cortisol in AM ( $<5$ ), Cushing’s is excluded
    - If high cortisol in AM, Cushing’s syndrome
  - c. ACTH level: if low, then primary (adrenal source); if high, then order high-dose dexamethasone suppression test
    - Below 50% suppression of cortisol: ectopic ACTH
    - Above 50% suppression of cortisol: Cushing disease
  - d. CRH stimulation test (alternative to high-dose dexamethasone suppression test)
    - Increase in ACTH/cortisol  $\rightarrow$  Cushing disease
    - No increase  $\rightarrow$  ectopic ACTH or adrenal tumor

#### B. Adrenal Insufficiency

1. Primary (Addison disease): low cortisol, high ACTH, no response to ACTH infusion
  - a. Autoimmune most common cause in industrialized nations
  - b. Infectious: TB (most common worldwide), fungal
  - c. Iatrogenic
  - d. Metastatic disease, typically lung or breast
2. Secondary: low cortisol, low/normal ACTH, responds to ACTH infusion
  - a. Iatrogenic (long-term steroid therapy) is most common
  - b. Hypopituitarism
3. Tertiary: hypothalamic disease (no CRH release)
4. Symptoms/signs
  - a. Hyperpigmentation in primary adrenal insufficiency due to co-secretion of melanocyte stimulating hormone with ACTH
  - b. Hypoaldosteronemia in primary adrenal insufficiency (leading to hyponatremia, hyperkalemia, hypovolemia, and hypotension)
  - c. Others: anorexia, abdominal pain, nausea/vomiting, hypoglycemia, lethargy

5. Diagnosis: ACTH (cosyntropin) stimulation test; insulin-induced hypoglycemia was previously used to assess adrenal insufficiency
  - a. ACTH stimulation test can diagnose adrenal insufficiency as well as quantify the degree of adrenal impairment; serum cortisol levels will increase after administration of cosyntropin in acute secondary adrenal insufficiency
    - The test will be abnormal in primary adrenal insufficiency and chronic secondary adrenal insufficiency (adrenals atrophied from chronic lack of stimulation)
6. Treatment: glucocorticoids (hydrocortisone, prednisone); if primary insufficiency, also need to provide mineralocorticoid (fludrocortisone)
7. Complications: adrenal crisis (life-threatening adrenal insufficiency with severe hypotension, abdominal pain, acute renal failure); treat with IV fluids and hydrocortisone

### C. Pheochromocytoma

1. 5P's: Pressure (HTN), Pain (headache, chest), Palpitations (tachycardia, tremor, fever), Perspiration, Pallor
2. Rule of 10's: 10% familial, 10% bilateral (MEN II), 10% malignant, 10% multiple, 10% children, 10% extra-adrenal
3. Diagnosis: urine (metanephrine, VMA, homovanillic acid, normetanephrine), plasma metanephrines; elevated epinephrine suggests adrenal source
4. Treatment:  $\alpha$ -blockade (phenoxybenzamine) first to control HTN, then add  $\beta$ -blockade; surgical resection is definitive treatment
5. Associated with MEN IIA/IIB, von Hippel Lindau, neurofibromatosis type 1

### D. Primary Hyperaldosteronism

1. Hypertension, hypernatremia, hypokalemia, metabolic alkalosis
2. Adrenal adenoma: can see in imaging (CT), on adrenal venous sampling will see unilaterally increased aldosterone level; treatment is resection
3. Adrenal hyperplasia: equal aldosterone levels bilaterally on venous sampling; treat with spironolactone

## IV. Diabetes Mellitus (Table 13-7)

### A. Acute Complications

1. Diabetic ketoacidosis (DKA)
  - a. Insulin deficiency and glucagon excess lead to hyperglycemia and ketogenesis, precipitated by stress or illness
    - Precipitants: lack of insulin (undiagnosed or forgot meds), infection, myocardial infarction, stroke, medications (e.g., steroids,  $\beta$ -blockers, etc.), intoxication
  - b. Symptoms/signs
    - Abdominal pain, nausea/vomiting, Kussmaul respirations, "fruity" breath, dehydration, polydipsia, polyuria, polyphagia, altered mental status
    - Hyperglycemia (400s to 800s), serum/urine ketones, anion gap metabolic acidosis

**Table 13-7 Comparison of Type 1 and Type 2 Diabetes Mellitus**

|              | Type I                                                                                                                                                                                              | Type II                                                                                                                                                                                                                                                   |
|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Associations | Sudden onset, young, thin, low endogenous insulin                                                                                                                                                   | Gradual onset, older, obese, starts with increased endogenous insulin but eventually progresses to normal/low                                                                                                                                             |
| Symptoms     | Polyuria, polydipsia, fatigue, blurry vision, recurrent fungal infections                                                                                                                           |                                                                                                                                                                                                                                                           |
| Diagnosis    | Any of the following:<br>1. Fasting blood glucose $\geq 126$ on two occasions<br>2. Glucose $\geq 200$ after 2 h OGTT (75 g)<br>3. Random glucose $\geq 200$ with symptoms<br>4. HbA1c $\geq 6.5\%$ |                                                                                                                                                                                                                                                           |
| Treatment    | Insulin                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>• Lifestyle changes (diet, exercise)</li> <li>• Metformin first-line treatment</li> <li>• Other oral hypoglycemics (sulfonylureas, thiazolidinediones, acarbose)</li> <li>• Insulin if advanced disease</li> </ul> |

- Hyperkalemia may be present, but total body potassium is low (from acidemia)

- Hyponatremia may be present due to hyperglycemia

c. Treatment

- Heavy IV fluids; once blood glucose reaches 250, add glucose
- IV insulin (caution for hypokalemia)
- Replete potassium, magnesium, phosphate

2. Hyperosmolar hyperglycemic nonketotic syndrome

- Insulin deficiency leads to hyperglycemia, which leads to osmotic diuresis and dehydration with hyperosmolality; the presence of some insulin prevents ketogenesis
- Symptoms/signs: polydipsia, polyuria, dehydration, CNS findings secondary to hyperosmolality; hyperglycemia ( $>900$ s), no ketosis
- Treatment: aggressive fluid resuscitation, insulin

## B. Chronic Complications

1. Microvascular

- Nephropathy: screen for microalbuminuria (albumin:creatinine ratio 30 to 300 mg/g or 30 to 300 mg/d albuminuria)
  - Treat with tight BP/glucose control, ACEI/ARBs (decreases the elevated intraglomerular pressure that occurs early in the disease)
- Retinopathy: hemorrhages, exudates, microaneurysms, edema; can have proliferative (neovascularization) or nonproliferative

disease; can also have vitreal hemorrhage and retinal detachment as complications

c. Neuropathy

- Peripheral: stocking/glove paresthesia, leads to burning pain or diabetic foot ulcers; treat with gabapentin, tricyclic antidepressants (TCAs)
- Mononeuropathies (median, ulnar, peroneal, cranial nerves)
- Autonomic neuropathy: impotence, neurogenic bladder, gastroparesis, postural hypotension

2. Macrovascular

- a. Atherosclerosis → CAD (most common cause of death in diabetic patients), CHF, peripheral vascular disease, stroke
- b. Treatment: reduce other risk factors

## V. Multiple Endocrine Neoplasia: extremely high yield!

- A. MEN I – 3P's: Parathyroid hyperplasia, Pancreatic islet cell tumor (ZES, insulinoma), Pituitary tumors
- B. MEN IIA – 2P's: Pheochromocytoma, hyperParathyroidism, medullary thyroid carcinoma
- C. MEN IIB – 1P: Pheochromocytoma, medullary thyroid carcinoma, Marfanoid body habitus, mucosal neuromas

## VI. Other Clinical Syndromes

### A. Hyperprolactinemia

1. Symptoms/signs: headache, bitemporal hemianopsia; in men: hypogonadism, decreased libido, impotence, galactorrhea/gynecomastia; in women: menstrual irregularities, dyspareunia, osteoporosis, galactorrhea
2. Etiologies: prolactinoma (most common), medications (psych meds, H2 blockers, metoclopramide, verapamil, estrogen), pregnancy, renal failure (decreased clearance), hypothyroidism (elevated TRH decreases dopaminergic inhibition of prolactin production and release)
3. Treatment: treat underlying cause
  - a. Prolactinoma: bromocriptine or cabergoline if symptomatic; surgical resection is possible, but high rate of recurrence

### B. Thyroid Nodule

1. Concern for cancer if young (<20) or old (>70), male, history of neck irradiation, hard/immobile nodule, cervical adenopathy
2. Workup (note: guidelines change, but shelf examination is not always up to date)
  - a. Start with TSH and ultrasound
    - If TSH low, scintigraphy; if "hot" nodule, likely benign; concerning if "cold" nodule
    - If TSH normal or high, then fine needle aspiration biopsy (FNAB) is the next step
    - Ultrasound provides more information about the thyroid anatomy and the risk of thyroid cancer
  - b. Scintigraphy: to determine whether a nodule is functioning

- Vast majority of “hot” (hyperfunctioning) nodules are benign; no FNAB necessary
  - “Cold” (hypofunctioning) nodules and indeterminate nodules should undergo FNAB
  - c. FNAB results
    - Benign: follow with repeat ultrasound or FNAB later
    - Indeterminate: options include repeating FNAB or surgery
    - Suspicious: surgery
    - Malignant: surgery
- C. Hypoglycemia**
1. *Whipple triad* (classically described for insulinoma): hypoglycemic symptoms, blood glucose  $<50$  at time of symptoms, and symptoms relieved with glucose
  2. Causes include drug-induced (e.g., insulin without eating), factitious (will have low C-peptide), insulinoma, idiopathic, adrenal insufficiency, liver failure
  3. Symptoms: elevated epinephrine leads to sweating, tremor, tachycardia, anxiety; decreased glucose to brain leads to behavioral changes, coma
  4. Treatment: sugar-containing foods, D50 W

## Infectious Diseases

*This is a very high yield section for the shelf examination. It is important to recognize many infectious diseases (e.g., pneumonia) while also knowing what the most common organisms are that cause the disease so that appropriate antibiotics can be started empirically (e.g., pneumonia – *S. pneumoniae* – macrolide or fluoroquinolone antibiotic). In many cases on the shelf examination, you must make an educated guess as to the diagnosis, most common organism, and so forth based purely on risk factors and epidemiology; this section is a good example of that principle. The most important, high-yield points to recognize for the shelf are summarized here. Understand, however, that this is an extremely broad topic and there is a possibility that an obscure infectious disease question will appear; in that case, make an educated guess and move on!*

### I. Empiric Antibiotic Regimens (Table 13-8)

### II. Infections of the Respiratory Tract

- A. Pneumonia:** suspect in patient presenting with fever, cough, productive sputum
1. Types
    - a. Community-acquired pneumonia (CAP): exclude the following definitions
    - b. Health care–associated pneumonia (HCAP): hospitalized  $>2$  days within 90 days of the pneumonia; also consider those in long-term care facility (nursing home), or receiving PO antibiotics, chemo, wound care, or hemodialysis

Table 13-8    Empiric Antibiotic Regimens for Various Infectious Diseases

| Infection  | Organisms                                                                                                                                                               | First-line Empiric Antibiotics                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pneumonia  | CAP: <i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Mycoplasma</i> , many others (see "Pneumonia" section below)                                                      | <ul style="list-style-type: none"><li>• Outpatient: macrolide or doxycycline<ul style="list-style-type: none"><li>▪ E.g., azithromycin</li></ul></li><li>• Inpatient: (anti-pneumococcal β-lactam + macrolide) or fluoroquinolone<ul style="list-style-type: none"><li>▪ E.g., ceftriaxone + clarithromycin</li></ul></li><li>• ICU level: anti-pneumococcal β-lactam + (macrolide or fluoroquinolone) + vancomycin<ul style="list-style-type: none"><li>▪ E.g., ceftriaxone + levofloxacin + vancomycin</li></ul></li></ul> |
|            | VAP/HAP/HCAP: GNRs ( <i>Pseudomonas</i> , <i>Klebsiella</i> , <i>E. coli</i> , <i>Stenotrophomonas</i> ), <i>S. aureus</i> (MSSA and MRSA), <i>Acinetobacter</i>        | <ul style="list-style-type: none"><li>• Without risk factors for MDR organisms: ampicillin-sulbactam or ceftriaxone or ertapenem or fluoroquinolone</li><li>• With risk factors for MDR organisms: anti-pseudomonal antibiotic + anti-MRSA + (fluoroquinolone or aminoglycoside)<ul style="list-style-type: none"><li>▪ E.g., piperacillin-tazobactam + vancomycin + gentamicin</li></ul></li></ul>                                                                                                                          |
|            | Aspiration PNA: oropharyngeal microbes                                                                                                                                  | <ul style="list-style-type: none"><li>• No consensus; clindamycin or amoxicillin-clavulanate are good options; metronidazole should not be used as monotherapy</li></ul>                                                                                                                                                                                                                                                                                                                                                     |
| Meningitis | <i>S. pneumoniae</i> , <i>N meningitides</i> , <i>H. influenzae</i> , <i>Listeria</i> (in really young and old), <i>S. aureus</i> (if recent neurosurgery or CSF shunt) | Ceftriaxone + vancomycin +/- ampicillin (+ acyclovir if concern for HSV encephalitis)                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Sepsis     | Enteric GNRs, <i>Pseudomonas</i> , Staph, <i>S. viridans</i> ... but depends on source                                                                                  | Ceftriaxone + gentamicin + metronidazole (in practice there are other options, but the key is to start very broad)                                                                                                                                                                                                                                                                                                                                                                                                           |



|                        |                                                                                                                                                                                                                                                      |                                                                                                                                            |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| Infective Endocarditis | <i>S. viridans</i> , <i>Enterococcus</i> , <i>S. aureus</i> , <i>S. epidermidis</i> , GNRs, HACEK, others ( <i>Bartonella</i> , <i>Coxiella</i> , <i>Chlamydia</i> , <i>Legionella</i> , <i>Brucella</i> )                                           | ABE: vancomycin +/- gentamicin<br>SBE: ceftriaxone + gentamicin<br>PVE: vancomycin + gentamicin +/- (cefepime or ceftriaxone)              |
| Cellulitis             | Staph, Strep                                                                                                                                                                                                                                         | Cephalosporin or PCNase-resistant PCN (vancomycin if concern for MRSA)                                                                     |
| Osteomyelitis          | <i>S. aureus</i> , TB (Pott disease), <i>S. epidermidis</i> (after ortho surgery), polymicrobial, <i>Pseudomonas</i> (in diabetic foot), <i>Salmonella</i> (sickle cell patient)                                                                     | Oxacillin or vancomycin (but should be based on culture data; empiric fluoroquinolone or anti-pseudomonal can be used in certain patients) |
| UTI (cystitis)         | <ul style="list-style-type: none"> <li>Uncomplicated: <i>E. coli</i>, <i>Proteus</i>, <i>Klebsiella</i>, <i>S. saprophyticus</i></li> <li>Complicated: <i>E. coli</i>, enterococci, <i>Pseudomonas</i>, <i>S. epidermidis</i>, other GNRs</li> </ul> | Ciprofloxacin, trimethoprim-sulfamethoxazole, nitrofurantoin                                                                               |
| Neutropenic fever      | Enteric GNRs, <i>Pseudomonas</i> , <i>S. aureus</i> (MRSA), <i>S. viridans</i>                                                                                                                                                                       | (Imipenem or piperacillin or cefepime) +/- vancomycin or ceftazidime +/- vancomycin                                                        |

ABE, acute bacterial endocarditis; CAP, community-acquired pneumonia, GNR, gram negative rod, HACEK: *Haemophilus parainfluenzae*, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella*; HCAP, health care-associated pneumonia; MDR, multi-drug resistant; PCN, penicillin; PNA, pneumonia; PVE, prosthetic valve endocarditis; SBE, subacute bacterial endocarditis; VAP, ventilator-associated pneumonia.

- c. Hospital-acquired pneumonia (HAP): occurring 48 hours or more after admission
- d. Ventilator-associated pneumonia (VAP): occurring 48 hours or more after intubation
- e. Aspiration pneumonia: occurs 24 to 72 hours after aspiration event (aspiration pneumonitis is immediate)
- 2. Diagnosis: need CXR to diagnose; send sputum for gram stain and culture to narrow antibiotics
- 3. What bug is responsible?
  - a. Pneumonia in COPD patients: *H. influenzae*, *M. catarrhalis*
  - b. Elderly patient with diarrhea and hyponatremia: *Legionella* (look for water source in question stem, smoker, immunocompromised)
  - c. Alcoholics or elderly nursing home residents: *Klebsiella* and other gram-negative rods (GNRs)
    - Currant jelly sputum, think *Klebsiella*
  - d. Elderly patient with flu-like symptoms a week ago now with worsening respiratory symptoms and productive sputum: *S. aureus* (postviral infection)
  - e. Young, healthy patient with mild symptoms but CXR showing pneumonia: *Mycoplasma*, *Chlamydia*, viral
    - *Mycoplasma* is associated with cold agglutinins
  - f. Cystic fibrosis patient: *Pseudomonas*
  - g. Most common cause of pneumonia in HIV patient: *S. pneumoniae* (trick question, but always consider PCP)
    - Other bugs to consider: *H. influenzae*, TB, *E. coli*, *Klebsiella*, fungi (*Cryptococcus*, *Histoplasma*), CMV, *Toxoplasma*
- 4. Hints: do not need to memorize CURB-65 or *Pneumonia Severity Index*

### III. Infections of the Cardiovascular System

- A. **Infective Endocarditis:** always consider in patient with fever of unknown origin (FUO)
  - 1. Presentation: always consider in IV drug user with fever and new murmur, consider in patient with fever and imaging showing multiple emboli in lungs (right-sided endocarditis) or brain (left-sided endocarditis)
    - a. Acute bacterial endocarditis: virulent organism causing rapid onset of symptoms and severe disease (*S. aureus*, *S. pyogenes*, *S. pneumoniae*)
    - b. Subacute bacterial endocarditis: less virulent organism causing indolent infection (*S. viridans*)
  - 2. Diagnosis: based on *Duke Criteria* (do not need to memorize, just get the general picture of the risk factors): 2 major, 1 major + 3 minor, or 5 minor
    - a. Major: (+) blood culture by organism known to cause endocarditis, endocardial involvement (new valvular regurgitation or (+) echo findings)
    - b. Minor: predisposing condition (abnormal valve, high risk of bacteremia), fever, vascular phenomena (septic emboli, mycotic

aneurysms, intracranial hemorrhage [ICH], Janeway lesions), immune phenomena (Osler nodes, Roth spots, (+) rheumatoid factor, glomerulonephritis), (+) blood culture not meeting major criteria

3. Treatment: antibiotics usually for 4 to 6 weeks; start with empiric (Table 13-8), then narrow based on culture data; for IV drug user, always give vancomycin (covers MRSA); know that *S. viridans* is susceptible to penicillin
4. Hints: if *S. bovis* endocarditis, do a colonoscopy (associated with colon cancer)

**B. Pericarditis/Myocarditis:** think Coxsackie A/B, echovirus, treat with NSAIDs + colchicine

#### IV. Infections of the GI Tract

##### A. Diarrhea

1. Acute (<4 weeks)
  - a. Inflammatory (positive fecal leukocytes and blood)
    - Bacteria, in order of frequency: *Campylobacter* (chicken and milk, can be carried by puppies, can lead to Guillain-Barré syndrome and reactive arthritis); *Salmonella* (nontyphoidal: eggs and chicken, can produce bacteremia or chronic carrier state; *S. enterica* serovar *typhi* is the species that produces typhoid that presents with fever, bradycardia, “pea-soup” diarrhea, and a rose spot rash), *Shigella* (very contagious, seen often in daycares), *E. coli* (O157:H7, undercooked meat, can cause HUS in children)
      - Note: both *Campylobacter* and *Yersinia enterocolitica* can mimic appendicitis
    - Viruses: mostly think of viruses as causing noninflammatory diarrhea except CMV in immunocompromised patients
    - Parasites: most high yield is *Entamoeba histolytica*, which will present in a recent traveler (e.g., recently went on a trip to Mexico); can cause liver abscess
  - b. Noninflammatory
    - Food poisoning: caused by pre-formed toxin and lasts less than 24 hours; think *S. aureus* (meat and dairy), *B. cereus* (reheated rice), *C. botulinum* (canned foods), or *C. perfringens* (meat)
    - Viruses: norovirus (lasts 1 to 2 days; daycares and cruise ships), rotavirus (mostly children), adenovirus, astrovirus
    - Parasites: *Cryptosporidium* (most common, often in HIV patients or immunosuppressed, can produce chronic diarrhea), *Giardia* (unsanitary water, seen in travelers, camping/hiking, immunocompromised)
  - c. When to treat: oral rehydration sufficient in most cases; treat with fluoroquinolone in patients with moderate/severe traveler’s diarrhea or with fever and bloody diarrhea; if *Campylobacter* suspected, use macrolide; if *E. coli* O157:H7, do *not* give antibiotics (may increase risk of HUS)

- 2. Chronic (>4 weeks): less likely to be infectious, but infectious organisms include *Tropheryma whipplei* (Whipple disease, can present with fever, arthritis, valvular disease, and skin pigmentation; positive PAS stain on histology, needs long-term antibiotic treatment), *C. difficile* (see below), *Campylobacter*, *Cryptosporidium*, TB, CMV, *Giardia*, *Strongyloides* (also look for pulmonary symptoms with eosinophilia; treat with ivermectin or albendazole)
  - a. Quick overview of other causes of chronic diarrhea: medications, IBD, irritable bowel syndrome (IBS; abdominal pain  $\geq 3$  d/mo for at least 3 months + either improvement in symptoms after defecation or change in frequency of stool at onset or change in form of stool at onset), celiac disease (immune reaction to gluten, associated with dermatitis herpetiformis, diagnose with antitissue transglutaminase or anti-endomysial antibodies, or biopsy showing triad of crypt hyperplasia, villous atrophy, and intraepithelial lymphocytosis), pancreatic insufficiency (chronic pancreatitis, pancreatic cancer, cystic fibrosis), lactose intolerance (diagnose with hydrogen breath test), hormones (gastrin in ZES, VIP in VIPoma, glucagon), laxative abuse, mesenteric ischemia, colorectal cancer, Addison disease, and many others
    - Can check stool for osmotic gap to differentiate osmotic diarrhea (e.g., lactose intolerance, malabsorption) from secretory/motility disorders (e.g., hormones, IBS)

**B. Viral Hepatitis**

- 1. Hepatitis A and E: fecal–oral transmission, self-limited; hepatitis E has an increased mortality in pregnant patients
- 2. Hepatitis B: most questions involve an interpretation of serology tests; infection is from blood, sexual, or perinatal transmission
  - a. Associations: cirrhosis (increased risk with HCV, HDV, or HIV co-infection), hepatocellular carcinoma (HCC), polymyalgia rheumatica, membranoproliferative glomerulonephritis, and polyarteritis nodosa
  - b. Diagnosis based on serology (Table 13-9): hepatitis B surface antigen (HBsAg) is the hallmark of infection; hepatitis B e antigen

**Table 13-9 Serologic Markers in the Diagnosis of HBV Infection**

|                   | HBsAg | Anti-HBs | Anti-HBc | HBeAg | Anti-HBe |
|-------------------|-------|----------|----------|-------|----------|
| Immunized         | –     | +        | –        | –     | –        |
| Acute infection   | +     | –        | IgM      | +     | –        |
| Cleared infection | –     | +        | IgG      | –     | –        |
| Chronic infection | +     | –        | IgG      | +/–   | +/–      |
| Window period     | –     | –        | IgM      | +/–   | +/–      |

(HBsAg) correlates with disease activity and infectivity; hepatitis B core antigen (HBcAg) exists within hepatocytes and is not detected in the serum; antibodies to HBsAg (anti-HBsAg) indicate immunity; antibodies to HBcAg (anti-HBcAg) indicates exposure to HBV but does not indicate immunity

- c. Treatment: not all patients need treatment and choosing the agent and when to treat is beyond the scope of the examination; however, options include interferon, lamivudine, tenofovir, and others
3. Hepatitis C: infection is usually from blood transmission (more than sexual transmission); progresses to chronic infection more often than HBV
  - a. Associations: membranoproliferative glomerulonephritis, cryoglobulinemia, non-Hodgkin lymphoma, idiopathic pulmonary fibrosis
  - b. Treatment: pegylated interferon + ribavirin; newer agents with high cure rates (e.g., sofosbuvir, ledipasvir) are unlikely to show up on the examination for many years
4. Hepatitis D: requires HBV infection, can exacerbate existing liver disease, progressing to cirrhosis

### C. Pseudomembranous colitis (*C. difficile* colitis)

1. Presentation: patient who was recently started on (any) antibiotics (although clindamycin was previously a shelf favorite), now with severe watery and foul-smelling diarrhea; fever, leukocytosis
2. Complications: toxic megacolon, perforation, anasarca (from electrolyte disturbances)
3. Treatment: metronidazole (PO or IV), vancomycin (PO); do not give loperamide to improve diarrhea

## V. Infections of the Nervous System

### A. Meningitis: suspect in patient with fever, headache, nuchal rigidity, photophobia, altered mental status

1. Diagnosis: on examination, look for Kernig/Brudzinski (specific, not sensitive; jolt test is more sensitive), focal neurologic findings, rash; however, will almost certainly see lumbar puncture (LP) findings (Table 13-10) to make the diagnosis
  - a. Other findings: increased opening pressure in bacterial, TB, or fungal; if lots of RBCs after LP, possibly traumatic tap but also consider HSV encephalitis
  - b. If concern for increased intracranial pressure (ICP), do CT before LP
2. Treatment: see empiric treatment above; dexamethasone useful only with *S. pneumoniae*
  - a. Prophylaxis: close contacts of meningococcal meningitis, give rifampin (or ciprofloxacin or ceftriaxone)

### B. Encephalitis: inflammation of brain parenchyma, many causes

1. Viral: enteroviruses (Coxsackie, echo), HSV, VZV, HIV, mumps, CMV, EBV, JC virus, arboviruses (West Nile, Eastern/Western equine, etc.)

**Table 13-10 CSF Findings After Lumbar Puncture in Meningitis**

|           | WBCs              | Protein  | Glucose |
|-----------|-------------------|----------|---------|
| Normal    | 0–5               | 15–40    | 50–75   |
| Bacterial | ↑↑↑<br>PMNs       | ↑↑       | ↓       |
| Viral     | ↑<br>lymphocytes  | ↑        | Normal  |
| Fungal    | ↑<br>lymphocytes  | Normal/↑ | ↓       |
| TB        | ↑↑<br>lymphocytes | ↑↑       | ↓       |

- a. Diagnose with LP, treat with acyclovir (HSV or VZV) or ganciclovir +/- foscarnet (CMV)
- 2. Hints: MRI showing inflammation of temporal lobe = HSV encephalitis

**VI. Infections of the Genitourinary System**

**A. Lower UTI** (urethritis, cystitis)

- 1. Complicated: UTI in men, pregnant women, UTI with underlying structural disease or immunosuppression
- 2. Diagnosis: just look for symptoms (dysuria, urgency, frequency, suprapubic discomfort) with UA findings (pyuria + bacteriuria +/- hematuria +/- nitrites)
- 3. For urethritis, treat for both *Neisseria* and *Chlamydia*: ceftriaxone + (doxycycline or azithromycin)
- 4. Hints: *S. saprophyticus* if young woman and recent onset sexual activity

**B. Pyelonephritis:** on shelf, will present as fever, flank pain, costovertebral angle (CVA) tenderness, pyuria; look out for sepsis as a complication

- 1. Treatment: ciprofloxacin or cephalosporin if outpatient; ceftriaxone, ciprofloxacin, gentamicin, or ampicillin/sulbactam if inpatient

**VII. Sexually Transmitted Infections (STIs)**

**A. Chlamydia:** most common bacterial STI, may be asymptomatic or present with purulent urethral discharge

- 1. Treatment: azithromycin or doxycycline (do not need to cover for gonorrhea, since it is much less common); treat sexual partners
- 2. Important complications: pelvic inflammatory disease (PID) in women, which is a common cause of infertility

**B. Gonorrhea:** may be asymptomatic or present with purulent urethral discharge; look for gram-negative diplococci within neutrophils

1. Treatment: ceftriaxone + azithromycin (to cover for *chlamydia*, which commonly coinfects and is much more common than gonorrhea); treat sexual partners
  2. Important complications: PID, Fitz-Hugh-Curtis, disseminated infection (will present with migratory polyarthritides +/- pustular rash)
- C. Syphilis:** spirochete infection, primary infection presents as painless chancre, secondary stage with systemic flu-like symptoms and maculopapular rash, tertiary stage with gummas, neurosyphilis (including tabes dorsalis), or cardiovascular disease (aortitis)
1. Treatment is simple with one dose of IM or IV penicillin; common question on shelf is a patient who is allergic to penicillin with syphilis – there are alternative treatments, but penicillin is the only proven treatment with data, so the correct answer in many scenarios (esp. high risk patients like pregnant women) is penicillin desensitization followed by treatment with penicillin
- D. Herpes Simplex Virus (HSV):** HSV-1 responsible for most cold sores, HSV-2 responsible for most genital lesions; genital lesions present as vesicles on an erythematous base (“dew drops on a rose petal”), can diagnose with many methods (Tzanck smear, culture, PCR, etc.); treatment is acyclovir
1. Also know that HSV can cause keratoconjunctivitis; look for picture of corneal dendrite or mention of this in the vignette (do *not* give topical steroids in this case)
- E. Human Papillomavirus (HPV):** virus that causes anogenital warts (types 6, 11) and cervical cancer (types 16, 18, 31, 45); HPV vaccine directed against types 6, 11, 16, 18

## VIII. HIV/AIDS

- A. AIDS Definition:** HIV infection + CD4 <200 or opportunistic infection or malignancy
- B. Acute Infection:** suspect in just about every patient on the shelf (if HIV is an answer choice, probably the right choice); nonspecific presentation, but may present as mononucleosis-like syndrome
- C. Diagnosis:** ELISA (very sensitive); if positive, follow with Western blot (very specific); PCR to follow viral load
- D. Important Opportunistic Infections**
1. Lungs: PCP, TB, fungi
    - a. PCP pneumonia: CXR shows bilateral, diffuse infiltrates; may see elevated LDH; treat with trimethoprim-sulfamethoxazole (treat with steroids before if PaO<sub>2</sub> <70 or A-a gradient >35)
  2. GI: diarrhea caused by CMV colitis, MAC, *Cryptosporidium*
  3. Skin: Kaposi sarcoma (HHV-8), bacillary angiomatosis (*Bartonella*)
  4. Eyes: CMV retinitis
  5. Renal: HIV causes FSGS
  6. Heme/onc: anemia, leukopenia, thrombocytopenia, CNS lymphoma, cervical and anal cancers, non-Hodgkin lymphoma
  7. Neurologic: meningitis (*Cryptococcus*), toxoplasmosis, PML, AIDS dementia complex, peripheral neuropathy

8. By CD4 count
  - a. Below 400: oral thrush, tinea pedis, VZV reactivation, TB reactivation, other bacteria (*H. influenzae*, *S. pneumoniae*, *Salmonella*)
  - b. Below 200: HSV reactivation, cryptosporidiosis, *Isospora*, disseminated coccidioidomycosis, PCP, *Bartonella*, *Cryptococcus*, *Histoplasma*
  - c. Below 100: Candidal esophagitis, toxoplasmosis, *Nocardia* brain abscess
  - d. Below 50: CMV retinitis and esophagitis, disseminated MAC, cryptococcal meningoencephalitis, invasive aspergillosis, bacillary angiomatosis, CNS lymphoma, PML
- E. **Treatment:** 2 NRTIs + [NNRTI or PI or INSTI], (NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor)
  1. Good first regimen in treatment-naïve patient: tenofovir–emtricitabine (2 NRTI combination) + efavirenz (NNRTI)
    - a. Use rilpivirine or nevirapine (NNRTIs) or a PI instead of efavirenz if patient is pregnant or desiring pregnancy
  2. When to start treatment: some debate on this topic, but many recommend treating all patients with confirmed HIV infection; all patients with a CD4 count <350 should definitely be treated
    - a. US guidelines recommend treatment at any CD4 count; there is no mortality benefit at higher CD4 counts, but lower morbidity with prevention of new infections
  3. Ritonavir (a PI that induces CYP 1A2 and inhibits CYP 3A4 and 2D6) can be used to boost serum concentration of another PI, increasing efficacy and decreasing resistance
  4. Important toxicities: pancreatitis (didanosine), hypersensitivity reaction (abacavir), lactic acidosis (any NRTI), Stevens–Johnson syndrome (NNRTIs), liver failure (nevirapine), crystal nephropathy (indinavir), truncal obesity and hyperlipidemia (PIs), bone marrow suppression (zidovudine), CNS effects such as depression and psychosis (efavirenz)
- F. **Prophylaxis:** start trimethoprim–sulfamethoxazole when CD4 <200 (PCP), azithromycin when CD4 <50 (MAC)
  1. Other options for PCP prophylaxis: dapsone, atovaquone, pentamidine
    - a. Dapsone toxicities: hemolysis (especially with G6PD deficiency), methemoglobinemia, agranulocytosis, dermatologic reactions (e.g., Stevens–Johnson syndrome)
  2. Trimethoprim–sulfamethoxazole also covers *toxoplasmosis* (needed when CD4 <100, but should already be receiving for PCP prophylaxis)

## IX. TB

- A. **Risk Factors:** immigrant, homeless, jail exposure, health care worker, HIV, chronic renal failure, DM, organ transplant, IV drug use, alcoholic, taking biologics (rituximab, TNF- $\alpha$  inhibitors)



- B. Screening:** PPD, examine 48 to 72 hours later (delayed type IV hypersensitivity reaction); if PPD (+), order CXR and if active do sputum studies (acid fast stain, culture, etc.)
  - 1. Above 15 mm induration: (+) in everyone
  - 2. Above 10 mm: (+) in high risk, high prevalence populations (risk factors above)
  - 3. Above 5 mm: (+) in HIV or immunosuppressed, close contact to active TB patient, CXR with apical findings consistent with TB
- C.** Another screening option is an interferon- $\gamma$  release assay, which has a high sensitivity for latent TB and is not affected by BCG vaccination; cannot differentiate latent from active TB
- D.** Presentations include primary TB pneumonia (middle/lower lobe consolidation), reactivation TB (apical infiltrate), miliary TB (constitutional symptoms, small “millet-seed” like lesions in lungs), extrapulmonary TB (pericarditis, meningitis, osteomyelitis, etc.)
- E. Treatment**
  - 1. Active TB: isolation, then “4 for 2 then 2 for 4” of **RIPE** treatment (Rifampin, Isoniazid, Pyrazinamide, Ethambutol for 2 months then rifampin and isoniazid for 4 months)
    - a. Note: there is a growing incidence of resistant TB infection and the treatment regimen differs, but this is unlikely to show up on the examination
  - 2. (+) PPD but no active disease: isoniazid + pyridoxine for 6 to 9 months
  - 3. Know these toxicities
    - a. Rifampin: orange body fluids, hepatitis, CYP450 inducer
    - b. Isoniazid: peripheral neuropathy (always give B<sub>6</sub> supplement), hepatitis, lupus-like syndrome
    - c. Pyrazinamide: hepatitis, hyperuricemia
    - d. Ethambutol: optic neuritis

## X. Sepsis

### A. Definitions

- 1. Systemic inflammatory response syndrome (SIRS; need 2/4): (1) temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ , (2) heart rate  $>90$  beats per minute, (3) respiratory rate  $>20$  breaths per minute (or  $\text{PaCO}_2 <32$ ), (4) WBC  $>12,000$  or  $<4,000$  or  $>10\%$  bands
- 2. Sepsis: SIRS with suspected infection
- 3. Severe sepsis: sepsis with end-organ dysfunction
- 4. Septic shock: sepsis with persistent hypotension despite fluid resuscitation

- B. Management:** early IV fluids, empiric antibiotics, source control (remove catheters, lines, etc.)

## XI. Miscellaneous Associations

### A. Infection of a Burn: *Pseudomonas*

- 1. Dog or cat bite: *Pasteurella multocida*, can present with fever and wound infection progressing to osteomyelitis, septic arthritis, or bacteremia; treat with amoxicillin-clavulanate (also used as prophylaxis in animal and human bites)

2. Cat scratch disease (regional lymphadenopathy): *Bartonella henselae*, presents with regional lymphadenopathy
3. Patient with fever, pulmonary symptoms, and a widened mediastinum on CXR: anthrax (*Bacillus anthracis*)
4. Patient with exposure to animal placentas: Q fever (*Coxiella burnetii*), exists as acute and chronic forms; can cause pneumonia, hepatitis, endocarditis, and affect the fetus during pregnancy
5. Sheep farmer with fever, night sweats, arthralgias, and hepatosplenomegaly: brucellosis (*Brucella* species); in women, can cause spontaneous abortion
6. Patient with exposure to dead animals, rabbits, or ticks who develops fever, headache, myalgias, and a papulo-ulcerative lesion with lymphadenopathy: tularemia (*Francisella tularensis*), specifically the ulceroglandular form of the disease (most common, but many other forms)
7. Parasite causing bladder cancer: *Schistosoma haematobium*; look for patient from endemic area (e.g., Egypt) presenting acutely with “swimmer’s itch” and progressing to a chronic form (other *Schistosoma* species can involve intestines and liver)
8. Hiker from the Eastern US with flu-like symptoms (+/- rash) and leukopenia, thrombocytopenia, and elevated AST/ALT: ehrlichiosis (*Ehrlichia chaffeensis*) or anaplasmosis (*Anaplasma phagocytophilum*) from tick bite; treat with doxycycline
9. Bell palsy: *Borrelia burgdorferi* (Lyme disease); treat with doxycycline
10. Gardener pricked by thorn with ascending lymphangitis: *Sporothrix schenckii*, treat with itraconazole or potassium iodide
11. Patient with tick bite and rash starting on hands and feet and spreading centrally: Rocky Mountain spotted fever from *Rickettsia rickettsii*, treat with doxycycline

## Hematology and Oncology

Questions relating to this topic are common on the examination, but primarily cover topics such as anemia and coagulation disorders. Leukemias and lymphomas may show up but are not as heavily tested as many fear they will be.

### I. Anemia

#### A. Approach to Anemia

1. Reticulocyte index
  - a. Above 2% suggests adequate response by bone marrow, which implies blood loss or hemolytic anemia as the cause of the anemia
  - b. Below 2% suggests inadequate RBC production by bone marrow
2. Mean corpuscular value (MCV)
  - a. Low: microcytic anemia – suggests a problem synthesizing hemoglobin
  - b. High: macrocytic anemia – suggests a problem synthesizing DNA

3. Peripheral blood smear
  - a. Spherocytes: hereditary spherocytosis, autoimmune hemolytic anemia, ABO incompatibility, G6PD deficiency; hint: think of processes causing autoimmune destruction of RBC membrane
  - b. Schistocytes: intravascular hemolysis (DIC, HUS/TTP, mechanical valve)
  - c. Sickled RBCs: sickle cell anemia
  - d. Heinz bodies (RBC inclusions), “bite cells”: G6PD deficiency, thalassemia
  - e. Howell–Jolly bodies: nonfunctional (or removed) spleen
  - f. Dacryocytes (“teardrop-shaped”): myelofibrosis
  - g. Rouleaux formation: multiple myeloma
  - h. Target cells: thalassemia, liver disease

**B. Microcytic Anemia:** findings represented in *Table 13-11*

1. Iron-deficiency anemia
  - a. Causes
    - Blood loss (most commonly menstruation, but think GI blood loss if patient is male or postmenopausal female; concern for colon cancer)
    - Dietary deficiency (6 months to 3 years if breastfed, adolescents, pregnancy)
  - b. Diagnosis: see *Table 13-11*; obtain stool guaiac or colonoscopy if GI bleed suspected (microcytic anemia in men or in the elderly, think colon cancer!)
  - c. Treat with oral or parenteral iron
2. Thalassemia
  - a. For the IM shelf, know the differences between the various thalassemias and which are transfusion-dependent; consider thalassemia minor if a patient with what looks like iron-deficiency anemia is not responding to iron therapy
  - b.  $\beta$ -thalassemia: inadequate production of  $\beta$ -chains, which leads to excess  $\alpha$ -chains to accumulate and damage the RBC membrane (hereditary, found in Mediterranean and Indian families)
    - One mutated  $\beta$ -gene:  $\beta$ -thalassemia minor  $\rightarrow$  mild anemia, no treatment necessary
    - Two mutated  $\beta$ -genes:  $\beta$ -thalassemia major  $\rightarrow$  severe anemia, elevated HbF and HbA<sub>2</sub>, target cells on smear, hepatosplenomegaly, expansion of marrow

**Table 13-11** Lab Findings in Various Microcytic Anemias

|                 | Serum Ferritin | Serum Fe                    | TIBC     | RDW      |
|-----------------|----------------|-----------------------------|----------|----------|
| Iron deficiency | ↓              | ↓                           | ↑        | ↑        |
| Chronic disease | Normal/↑       | ↓                           | Normal/↓ | Normal   |
| Thalassemia     | Normal/↑       | Normal (tx $\rightarrow$ ↑) | Normal   | Normal/↑ |

- Transfusion-dependent, often suffer from iron overload (hemochromatosis-like symptoms/signs)
    - c.  $\alpha$ -thalassemia: decrease in  $\alpha$ -chains, which causes  $\beta$ -chains to form tetramers
      - One mutated  $\alpha$ -gene:  $\alpha$ -thalassemia carrier  $\rightarrow$  silent
      - Two mutated  $\alpha$ -genes:  $\alpha$ -thalassemia minor  $\rightarrow$  mild anemia (common in African Americans), no treatment necessary
      - Three mutated  $\alpha$ -genes: HbH disease  $\rightarrow$  hemolytic anemia, splenomegaly
        - Often transfusion-dependent; splenectomy can help
      - Four mutated  $\alpha$ -genes: not compatible with life (hydrops fetalis)
  - 3. Sideroblastic anemia
    - a. Abnormality in RBC iron metabolism, either hereditary or acquired
    - b. Causes of acquired sideroblastic anemia include drugs (chloramphenicol, INH, alcohol), lead, collagen vascular disease, neoplasms (myelodysplastic syndromes)
    - c. Ringed sideroblasts in the bone marrow
    - d. Treatment: treat reversible causes, may give trial of pyridoxine
- C. Normocytic Anemia**
1. Anemia of chronic inflammation (microcytic or normocytic)
    - a. Causes: chronic infections (TB), neoplasms, inflammation (RA, SLE), trauma
    - b. Treat underlying process
  2. Aplastic anemia
    - a. Presents with pancytopenia
    - b. Causes: idiopathic (majority), radiation, medications (chloramphenicol, sulfonamides, gold, carbamazepine), viral infection (parvovirus B19, hepatitis B/C, EBV, CMV, HZV, HIV), chemicals (insecticides)
    - c. Bone marrow biopsy is definitive diagnostic test (hypocellular marrow)
    - d. Treat with transfusion if necessary and bone marrow transplantation
- D. Macrocytic Anemia:** vitamin B<sub>12</sub> or folate deficiency
1. Look for stomatitis, glossitis ("beefy red tongue") on examination
  2. Vitamin B<sub>12</sub> (cobalamin) deficiency
    - a. Differentiation from folate deficiency
      - Neuropathy causing subacute combined degeneration of the spinal tract (demyelination in posterior columns, lateral corticospinal tracts, spinocerebellar tracts leading to loss of position/vibratory sense in lower extremities, ataxia, upper motor neuron signs), as well as dementia
      - Elevated homocysteine and methylmalonic acid (only homocysteine is elevated in folate deficiency)
      - With dietary deficiency, folate is depleted faster than vitamin B<sub>12</sub>

- b. Causes: pernicious anemia (autoimmune disorder leading to lack of intrinsic factor), gastrectomy, ileal disease (Crohn disease, ileal resection), poor nutrition (alcoholism, strict vegetarianism)
- c. Smear can show hypersegmented neutrophils
- d. Schilling test
  - IM unlabeled B<sub>12</sub> (to saturate binding sites) + PO radioactive B<sub>12</sub>
  - Measure radioactive B<sub>12</sub> in urine and plasma (how much was absorbed)
    - If normal, then cause is dietary deficiency
    - If abnormal, pernicious anemia or malabsorption; further tests to distinguish
  - PO radioactive B<sub>12</sub> + PO intrinsic factor
  - Measure radioactive B<sub>12</sub> in urine and plasma
    - If improved from first measurement, then pernicious anemia is diagnosed
    - If still abnormal, then malabsorption with further workup for etiology
- e. Treat with IM vitamin B<sub>12</sub> (cyanocobalamin)
- 3. Folate deficiency
  - a. Causes: poor intake (most common cause; found in green vegetables), alcoholism, drugs (methotrexate, PO antibiotics, phenytoin), pregnancy, hemolysis, hemodialysis
  - b. Treat with daily PO folate supplementation
- 4. Other causes of microcytic anemia less tested: liver disease, alcoholism, hypothyroidism

### E. Hemolytic Anemia

- 1. High reticulocyte index, low haptoglobin, high LDH, unconjugated hyperbilirubinemia (leading to jaundice), hemoglobinuria (leading to dark urine)
- 2. Sickle cell anemia: autosomal recessive, mutant HbS replaces HbA (glu → val at sixth position)
  - a. Hemolytic anemia is normally well-compensated; however, can eventually lead to high-output heart failure
  - b. Aplastic crisis provoked by viral infection (typically parvovirus B19); treat with transfusion
  - c. Vaso-occlusive complications (often precipitated by decreased oxygen states, dehydration, infection, fever)
    - Pain crises (caused by ischemia in various organs, self-limited), acute chest syndrome (chest pain, pulmonary infiltrates, hypoxia), splenic sequestration crisis (sudden pooling of blood in spleen leads to splenomegaly and hypovolemic shock), priapism, strokes, ophthalmologic (retinal infarcts, vitreous hemorrhage, retinal detachment), chronic leg ulcers (classically over lateral malleoli), dactylitis (“sausage digits”)
  - d. Functional asplenia (usually by age 4) leads to increased susceptibility to infections by encapsulated organisms (*SHiN* organisms – *S. pneumoniae*, *H. influenzae*, *N. meningitidis*)

- While *Salmonella* osteomyelitis is more common in sickle cell patients than in the general population, *S. aureus* remains the most common cause of osteomyelitis in these patients
- e. Treatment
  - Vaccination against *S. pneumoniae*, *H. influenzae*, *N. meningitidis*
  - Prophylactic penicillin from 4 months to 6 years
  - Folic acid, hydroxyurea (antineoplastic drug that increases fetal hemoglobin)
  - Treat pain crises with hydration, pain control, oxygen if required
  - Consider blood transfusion in acute chest syndrome, stroke, prolonged priapism, decompensation
- 3. Hereditary spherocytosis: autosomal dominant
  - a. Causes loss of RBC membrane structural proteins (spectrin, ankyrin) leading to spherocytes that are consumed in the spleen
  - b. Diagnosis: osmotic fragility test, elevated MCHC
  - c. Direct Coombs is negative, differentiating this from autoimmune hemolytic anemia (AIHA)
- 4. Autoimmune hemolytic anemia (Table 13-12)
- 5. G6PD deficiency: X-linked recessive
  - a. Precipitants of hemolysis: drugs (sulfonamides, nitrofurantoin, primaquine, dimercaprol), fava beans, infection
  - b. Warning: G6PD levels can be normal during hemolytic episodes
  - c. On the shelf examination, think of G6PD if you have a man of Middle Eastern descent who develops symptoms/signs of hemolytic anemia and was recently treated for an infection; or recently took a trip to Africa and may have taken malaria prophylaxis

**Table 13-12 Comparison of Cold and Warm AIHA**

|            | Cold AIHA                                                                 | Warm AIHA                                                                                                                |
|------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Mechanism  | IgM, intravascular hemolysis                                              | IgG, extravascular hemolysis                                                                                             |
| Etiologies | Idiopathic or secondary to infection ( <i>Mycoplasma</i> , mononeuclosis) | Idiopathic or secondary to lymphomas/leukemias, malignancies, collagen vascular diseases, drugs ( $\alpha$ -methyl dopa) |
| Diagnosis  | Direct Coombs negative, cold agglutinin titer positive                    | Direct Coombs positive                                                                                                   |
| Treatment  | Avoid cold exposure, chemotherapy; NOT steroids                           | Steroids, splenectomy (if refractory to steroids), immunosuppression, folic acid                                         |

6. Paroxysmal nocturnal hemoglobinuria (PNH)
  - a. Acquired chronic intravascular hemolysis caused by deficiency of proteins that prevent complement-mediated lysis of cells
  - b. Also have pancytopenia and thrombosis of venous systems (e.g., Budd–Chiari, DVTs)
  - c. Diagnostic tests
    - Ham test, sugar water test (PNH cells lyse in acidified serum and sucrose)
    - Flow cytometry (most sensitive/specific)
  - d. Treatment: glucocorticoids, bone marrow transplant

## II. **Thrombocytopenia:** see chart in Misc section below for symptoms/signs

### A. **Immune/Idiopathic thrombocytopenic purpura**

1. Acute form in children, commonly after viral illness and resolves spontaneously
2. Chronic form in adult women aged 20 to 40 years, rarely resolves spontaneously
3. Diagnosis: isolated thrombocytopenia, increased megakaryocytes in marrow
4. Treat with corticosteroids, IVIG, splenectomy (in chronic)

### B. **Thrombotic thrombocytopenic purpura**

1. The distinction between TTP and HUS is somewhat unclear; most think of these two entities on a spectrum, with TTP being more severe than HUS
  - a. TTP = HUS (microangiopathic hemolytic anemia, thrombocytopenia, renal failure) + fever + AMS
2. Treatment: immediate plasmapheresis; steroids and splenectomy may be helpful

### C. **Heparin-induced thrombocytopenia (HIT)**

1. Decrease in platelet count by 50% after heparin administration
2. Aggregation of platelets leads to venous thromboses (PE, DVT)
3. Type 1: occurs <48 hours after starting heparin; heparin causes platelet aggregation, no treatment required
4. Type 2: occurs 3 to 12 days after starting heparin; heparin induced antibody-mediated platelet injury, stop heparin immediately (can give direct thrombin inhibitors)

## III. **Anticoagulation**

### A. **Heparin:** potentiates antithrombin leading to inhibition of factors Xa/IIa

1. Monitor with PTT, reverse with protamine sulfate
2. Low-molecular-weight heparins (LMWH): enoxaparin, dalteparin
  - a. Inhibit factor Xa as much as unfractionated heparin, but less effect on factor IIa and platelets (reduced risk of HIT)
  - b. Cannot be monitored

### B. **Warfarin:** vitamin K antagonist leading to decrease in factors II/VIII/IX/X, proteins C/S

1. Monitored by PT (INR): takes 4 to 5 days for anticoagulation effect to take place (so use heparin bridge, or else potential adverse effect is warfarin-induced skin necrosis)

2. Teratogenic (heparin is not)
3. Reverse with vitamin K; this takes days, so administer FFP for immediate effect

#### IV. Coagulation Disorders

##### A. Von Willebrand Disease: autosomal dominant

1. Most common inherited bleeding disorder; presents similarly to thrombocytopenia
2. Diagnosis: prolonged bleeding time, decreased von Willebrand Factor (vWF), decreased factor VIII activity
3. Treatment: ddAVP (desmopressin), factor VIII concentrate after trauma/surgery

##### B. Hemophilia A: X-linked recessive deficiency in factor VIII

1. Diagnosis: low factor VIII level with normal vWF; prolonged PTT
2. Treatment: factor VIII concentrate; ddAVP in mild disease
3. Think of hemophilia A in a young boy with unexplained or recurrent hemarthroses

##### C. Hemophilia B: X-linked recessive deficiency in factor IX

1. Similar presentation to hemophilia A, but much less common
2. Treatment: factor IX concentrate (no role for ddAVP)

##### D. Disseminated Intravascular Coagulation

1. Causes: infection (especially gram-negative sepsis), obstetric (amniotic fluid emboli, retained dead fetus, abruptio placenta), major tissue injury (trauma, surgery), malignancy (acute promyelocytic leukemia, pancreas, lung, prostate), shock, snake venom
2. Leads to bleeding (especially if acute) in addition to thrombosis (especially if chronic)
3. Laboratory results
  - a. Increased PT, PTT, bleeding time, fibrin split products, D-dimer
  - b. Decreased fibrinogen, platelets
  - c. Schistocytes on smear
4. Treatment: treat underlying cause, administer FFP, platelets, cryoprecipitate as needed

##### E. Vitamin K Deficiency

1. Think about vitamin K deficiency in patients taking broad-spectrum antibiotics while NPO, patients on TPN, patients with malabsorption of fat-soluble vitamins (IBD, small bowel disease, obstructive jaundice)
2. Vitamin K replacement takes days to work, so administer FFP if needed for acute bleeding

##### F. Inherited Hypercoagulable States

1. Factor V Leiden: most common
2. Antithrombin III deficiency: these patients do not respond to heparin therapy
3. Proteins C/S deficiency

##### G. Acquired/Secondary Hypercoagulable States: malignancy, antiphospholipid antibody syndrome, pregnancy, immobilization (post-op, long plane rides, truck drivers), myeloproliferative disorders, OCPs, nephrotic syndrome, heart failure (leads to stasis of blood)



## V. Multiple Myeloma

- A. Plasma cell disorder with excessive light chain production
  1. **CRAB:** hyperCalcemia, Renal failure, Anemia (secondary to marrow infiltration), lytic bone lesions (leading to pathologic fractures, loss of height, bone pain)
  2. Infections secondary to loss of normal immunoglobulins
  3. Diagnosis: monoclonal spike (M protein) in serum or urine due to a single colony of IgG, urine with free light chains (Bence Jones protein), lytic bone lesions on x-ray, abnormal plasma cells on marrow biopsy, Rouleaux formation of RBCs on peripheral smear (“stack of coins”); elevated ESR, elevated creatinine, low WBCs and platelets
  4. Treatment: hematopoietic stem cell transplant; if patient unable to receive transplant, systemic chemotherapy followed by radiation therapy if no response to chemo

## VI. Lymphoma

- A. **Lymphoma versus Leukemia:** in general, both are cancers that arise from cells destined to become lymphocytes; however, lymphomas develop from cells in a lymph node or part of the lymphatic system whereas leukemias develop in cells in the bone marrow; there is overlap, and both lymphomas and leukemias can spread to involve the bone marrow or lymphatic system
- B. **Hodgkin Lymphoma**
  1. Bimodal age distribution (15 to 30 and >50)
  2. Symptoms/signs: painless lymphadenopathy (supraclavicular, cervical, axillary, mediastinal), B symptoms (fever, night sweats, weight loss), pruritus, cough
  3. Diagnosis
    - a. Lymph node biopsy: Reed Sternberg cells (owl’s eyes); inflammatory cell infiltrates that distinguish Hodgkin’s from non-Hodgkin’s; most common histologic type is nodular sclerosis
    - b. CXR or CT scan can show lymphadenopathy
  4. Treatment: chemotherapy and radiation therapy; specific chemo regimens not high yield for shelf, but specific chemo toxicities are high yield (see later)
- C. **Non-Hodgkin Lymphoma (NHL)**
  1. Much more common than Hodgkin; many types, but some examples include diffuse large B-cell lymphoma (most common adult NHL), Burkitt lymphoma (associated with EBV, endemic in Africa with jaw lesions, “starry sky” appearance on histology, may also present as acute leukemia), hairy cell leukemia (tartrate resistant acid phosphatase stain, treat with cladribine), mycosis fungoides (cutaneous T-cell lymphoma)
  2. Risk factors: HIV/AIDS, immunosuppression, EBV, HTLV-1, *H. pylori* gastritis (affects gut-associated lymphoid tissue), autoimmune disease (affects mucosa-associated lymphoid tissue)
  3. Symptoms/signs: painless firm lymphadenopathy (supraclavicular, axillary, cervical), B symptoms, hepatosplenomegaly (causing abdominal pain, fullness), recurrent infections

4. Diagnosis: lymph node biopsy
5. Treatment: can include observation, chemo (e.g., R-CHOP), or radiation

## VII. Leukemia

- A. **Acute:** rapid progression with blasts in marrow and blood stream; high white count with low blood counts of other marrow elements: anemia (fatigue), neutropenia (infections), and thrombocytopenia (bleeding)
  1. Acute lymphoblastic leukemia (ALL)
    - a. Most common malignancy in children <15
    - b. Very responsive to treatment; look for CALLA or TdT markers on immunohistochemistry in question stem
  2. Acute myelogenous leukemia (AML)
    - a. Mostly in adults: risk factors include radiation exposure, myeloproliferative syndromes, Down syndrome, chemotherapy
    - b. Acute promyelocytic leukemia: (15;17), Auer rods; treat with all-trans retinoic acid (complication of treatment includes DIC)
  3. Treatment: aggressive chemotherapy, if relapse then hematopoietic stem cell transplant (HSCT) an option
- B. **Chronic:** symptoms develop over a more prolonged period of time
  1. Chronic myeloid leukemia (CML)
    - a. Generally affects age range of 30 to 60, asymptomatic, found on routine blood tests, eventually progress to accelerated phase or blast crisis
    - b. Philadelphia chromosome, BCR-ABL fusion from t(9;22)
    - c. To differentiate CML from reactive leukocytosis, check for splenomegaly (present in CML), alkaline phosphatase activity (low in CML), and precipitating infection (absent in CML)
    - d. Diagnosis: marked leukocytosis (some blasts/promyelocytes), thrombocytosis, decreased leukocyte alkaline phosphatase activity
    - e. Treatment: imatinib (tyrosine kinase inhibitor)
  2. Chronic lymphocytic leukemia (CLL)
    - a. Typically affects adults >60, often asymptomatic
    - b. Diagnosis: marked leukocytosis (all mature lymphocytes), anemia, thrombocytopenia, neutropenia; peripheral smear shows smudge cells
    - c. Treatment: early stage can be followed without treatment; treatment is palliative
- C. Other high yield associations
  1. Older male with ruddy appearance, diffuse pruritus after hot shower: polycythemia vera, treat with phlebotomy
    - a. Also make sure polycythemia is not secondary (chronic smoker, lives at high elevation, etc.)
  2. Monoclonal IgM M-spike: Waldenstrom macroglobulinemia
    - a. Alternatively, if IgG M-spike with symptoms, multiple myeloma; if M-spike but no symptoms, then monoclonal gammopathy of undetermined significance (MGUS)

## VIII. Miscellaneous

## A. Transfusions

1. Packed RBCs: contain no platelet or clotting factors
  - a. Indications: low hemoglobin (can usually tolerate as low as 7, unless patient has another issue which interferes with oxygen delivery)
2. Fresh frozen plasma: contains clotting factors, but no blood cells
  - a. Indications: coagulopathy, high PT/PTT (e.g., supratherapeutic INR from warfarin therapy), deficiency of clotting factors
3. Cryoprecipitate: only contains factor VIII and fibrinogen
  - a. Indications: decreased fibrinogen (e.g., DIC), hemophilia A, vWD
4. Platelets
  - a. Indications: low platelets (for the shelf do not worry about exact values)
5. Transfusion reactions
  - a. Acute hemolytic reaction: caused by ABO-incompatibility
    - Occurs directly after initiation of transfusion
    - Fevers/chills, nausea/vomiting, back/flank/chest pain, dyspnea
    - Can lead to hypovolemic shock, DIC, renal failure
    - Treatment: *stop transfusion*, IV fluids, epinephrine for anaphylaxis, pressors to maintain BP if necessary
  - b. Delayed hemolytic reaction: caused by minor RBC antigens
    - Occurs 3 to 4 weeks after transfusion
    - Less severe than acute reaction: fever, jaundice, anemia
    - No treatment required
  - c. Transfusion Related Acute Lung Injury (TRALI)
    - Think of this in a patient who develops acute dyspnea 4 to 6 hours after transfusion of blood products
    - Infiltrates on CXR (may meet criteria for ALI or ARDS)

B. Thrombocytopenia versus impaired coagulation (*Table 13-13*)C. **Tumor Lysis Syndrome:** complication of chemo in acute leukemia and high-grade NHL

1. Rapid cell death → hyperkalemia, hyperuricemia, hyperphosphatemia

**Table 13-13 Clinical Manifestations of Thrombocytopenia and Coagulation Defects**

| Thrombocytopenia                                                                           | Impaired Coagulation    |
|--------------------------------------------------------------------------------------------|-------------------------|
| Cutaneous bleeding – petechiae/purpura                                                     | Hemarthroses            |
| Mucosal bleeding – epistaxis, heavy menstrual bleeding, hemoptysis, GI bleeding, hematuria | Hematomas               |
| Excessive bleeding after procedures                                                        | Intracranial hemorrhage |
| Intracranial hemorrhage                                                                    |                         |

**D. High-yield chemotherapy toxicities**

1. Patient with lymphoma develops lower abdominal pain and hematuria: hemorrhagic cystitis from cyclophosphamide/ifosfamide, prevent with mesna
2. NHL patient develops fatigue and shortness of breath 6 months after chemotherapy: heart failure from anthracycline cardiotoxicity (doxorubicin, daunorubicin); dexrazoxane is cardioprotective and may be used in the setting of high doses of anthracyclines
3. Patient with bladder cancer develops painful oral lesions and pancytopenia: methotrexate toxicity, which can cause mucositis, myelosuppression (can be reversed with leucovorin), and fatty liver
4. Patient with testicular cancer develops SOB and skin changes: bleomycin toxicity (causes pulmonary fibrosis); busulfan is another agent that causes pulmonary fibrosis
5. Weeks after finishing chemotherapy to treat a sarcoma, patient develops numbness and tingling in the extremities: peripheral neuropathy from vincristine
6. Patient with ovarian cancer develops progressive renal failure: cisplatin nephrotoxicity, which can be reduced with saline diuresis +/- amifostine (free radical scavenger, no strong evidence for use in current low dose cisplatin regimens); cisplatin can also cause neurotoxicity and ototoxicity
7. Breast cancer patient that later develops endometrial cancer: tamoxifen, which is a selective estrogen-receptor modulator (SERM) that acts as an estrogen receptor antagonist in breast tissue but an agonist in bone and endometrial tissue, increases the risk of endometrial cancer
8. Patient with CML and fluid retention: imatinib (tyrosine kinase inhibitor targeting BCR-ABL fusion protein), which can also cause cardiotoxicity; trastuzumab is a monoclonal antibody (targeting HER2/neu receptor in breast cancer) that also causes cardiotoxicity
9. Patient with a history of gout taking allopurinol and newly diagnosed cancer, major drug interactions to consider: allopurinol slows elimination of azathioprine and 6-mercaptopurine, increasing toxicity (6-thioguanine not affected)

## Rheumatology

*This section provides useful summaries of the differential diagnosis of arthritis, common rheumatologic conditions and how to diagnose and manage them, and the serum studies that aid in diagnosis. In practice these diseases overlap quite a bit (e.g., patient with symptoms of RA and Sjögren), but on the test they will be discreet entities.*

### **I. Arthritis** – first consider whether it affects one joint or multiple joints, and also if it is acute or chronic

- A. Monoarthritis:** consider septic joint, trauma, hemarthrosis, gout, pseudogout, first presentation of systemic disease that will later be polyarticular

1. Septic joint: always consider this diagnosis, since patients need early arthrocentesis and antibiotics or else permanent joint destruction can occur
    - a. *S. aureus* most common cause; other causes include *S. epidermidis*, *Streptococcus*, *N. gonorrhea*, *E. coli*, *Pseudomonas*, *Serratia*, Lyme disease (*B. burgdorferi*)
      - Base empiric antibiotics on gram stain: if gram (+), vancomycin; if gram (–) diplococci, ceftriaxone or cefotaxime; if gram (–) rods, ceftipime or piperacillin–tazobactam
  2. Gout: consider in patient with acute inflammation of a joint (commonly first metatarsophalangeal joint, ankles, knees); deposition of monosodium urate crystals due to acute change in serum uric acid concentration, tophi might be present
    - a. Treatment: acutely give NSAIDs or colchicine (may also consider steroids); for chronic treatment, give allopurinol/febuxostat or probenecid
      - Allopurinol and febuxostat inhibit xanthine oxidase, which reduces the production of uric acid; allopurinol toxicities include agranulocytosis, Stevens–Johnson syndrome, renal failure
      - Probenecid inhibits reabsorption of uric acid in the proximal convoluted tubule of the nephron; also inhibits secretion of penicillin
  3. Pseudogout: may present similarly to gout (but usually larger joints, especially knees), but vignette on examination will likely give joint fluid analysis (see below) to differentiate; caused by deposition of calcium pyrophosphate dihydrate (CPPD) crystals; may also see chondrocalcinosis on radiographs due to deposition of crystals in cartilage
    - a. Acute treatment similar to gout, chronic treatment is underlying cause (not high yield for examination)
- B. Oligoarthritis/Polyarthritis**
1. Older patient with joint pain involving distal interphalangeal joints (DIPs), worse after activity: osteoarthritis
  2. Young, sexually active patient with migratory polyarthritis with skin pustules: gonococcal arthritis (disseminated infection), treat with ceftriaxone (and consider adding doxycycline to cover *Chlamydia* empirically)
  3. Reactive arthritis: “can’t see, can’t pee, can’t climb a tree” (uveitis, urethritis, polyarthritis); seronegative, typically occurs after GU or GI infection (think *Chlamydia*, *Campylobacter*); may also see dactylitis, circinate balanitis, keratoderma blennorrhagica
  4. Systemic inflammatory conditions (SLE, RA, etc.; see below)
  5. Others: Lyme, viral (mother of kid with parvovirus B19 infection), psoriatic (“pencil-in-cup” deformity involving DIPs; look for typical skin lesions), IBD-associated
- C. Joint fluid analysis (Table 13-14)**

## II. Important Rheumatologic Conditions

Most importantly, know how to recognize the following conditions; if unsure how to treat the condition, best guess would be NSAIDs if mild,

**Table 13-14 Arthrocentesis Findings in Various Conditions**

|                     | Noninflammatory | Inflammatory                                                                                                                                                                                             | Septic                      |
|---------------------|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Appearance          | Clear           | Clear or opaque                                                                                                                                                                                          | Opaque                      |
| WBC/mm <sup>3</sup> | –/↑             | ↑↑ (>2,000)                                                                                                                                                                                              | ↑↑↑ (>50,000,<br>>75% PMNs) |
| Crystals            | None            | <ul style="list-style-type: none"><li>• Gout: needle-shaped crystals, (–) birefringence (yellow when parallel)</li><li>• Pseudogout: rhomboid crystals, (+) birefringence (blue when parallel)</li></ul> | None                        |

steroids if exacerbation, or heavy immunosuppressants if severe disease (e.g., cyclophosphamide, methotrexate, etc.)

**A. Systemic Lupus Erythematosus:** most common causes of death are infection and renal failure

1. Diagnosis: do not need to know specific diagnostic criteria for examination, just be able to recognize symptoms/signs
  - a. **SOAP BRAIN MD:** Serositis, Oral ulcers, Arthritis, Photosensitivity, Blood disorders (leukopenia, hemolytic anemia), Renal involvement, ANA, Immunologic phenomena (dsDNA, anti-Smith, antiphospholipid, etc.), Neurologic involvement (seizures, psychosis), Malar rash, Discoid rash
2. Antiphospholipid syndrome: may or may not occur in the context of SLE, etiologic antibodies include lupus anticoagulant, anticardiolipin, anti-β2 glycoprotein-I; look for recurrent miscarriages and thrombotic events (e.g., PE)
  - a. High yield: look for false (+) syphilis test! You might see a vignette with a woman experiencing multiple thrombotic events or obstetric complications testing (+) for syphilis; the “next step” would not be to treat for syphilis, it is likely a false (+) due to anticardiolipin antibodies
3. Drug-induced lupus: look for patient taking hydralazine or procainamide (less likely to be tested: isoniazid, pyrazinamide, quinidine, anti-TNF drugs, methyl dopa, diltiazem)
4. Treatment: not tested in detail, but NSAIDs, steroids, antimalarials (hydroxychloroquine; beware many drug toxicities including agranulocytosis, retinopathy, myopathy), other immunosuppressants (cyclophosphamide, mycophenolate, methotrexate, rituximab, etc.)

**B. Rheumatoid Arthritis**

1. Common symptoms/signs: look for symmetric pain and swelling of metacarpophalangeal joints (MCPs) and proximal interphalangeal

joints (PIPs), other joints involved as well with morning stiffness >1 hours, pannus formation with affected joints; also look for ulnar deviation, swan neck and boutonniere deformities, rheumatoid nodules on extensor surfaces

2. Extraarticular involvement: constitutional symptoms (fever, weight loss), eye involvement, ILD, pericarditis, blood abnormalities, renal disease
3. Treatment: NSAIDs and steroids, but also start disease modifying anti-rheumatic drugs (DMARDs; methotrexate, azathioprine, anti-TNF such as infliximab or etanercept, rituximab, etc.)
  - a. Screen for TB before starting infliximab and etanercept (reactivation TB)

**C. Scleroderma/Systemic Sclerosis:** two types, diffuse and limited (limited with better prognosis)

1. Diffuse systemic sclerosis: affects skin (scleroderma) and internal organs, including renal disease, GI disease, pericarditis and/or myocardial fibrosis, pulmonary fibrosis (most common cause of death)
2. CREST syndrome: Calcinosis, Raynaud's, Esophageal dysmotility, Sclerodactyly, Telangiectasias
  - a. Better prognosis than diffuse form, symptoms/signs more superficial with less internal organ involvement

**D. Sjögren Syndrome:** involvement of exocrine glands producing the symptoms of dry eyes, dry mouth, and enlarged parotid glands

1. Other findings include arthritis, renal involvement, vasculitis, pancreatitis
2. Treatment: NSAIDs, steroids, DMARDs, cyclosporine eyedrops

**E. Dermatomyositis/Polymyositis:** look for muscle weakness as the predominant symptom

1. If only muscle weakness, polymyositis; if skin also involved, dermatomyositis (look for shawl sign, heliotrope rash, and Gottron papules)
2. Diagnose with electromyography (EMG), muscle biopsy; treat with steroids, DMARDs, IVIG
3. May have associated malignancy; other organs affected include lungs (ILD), heart (myocarditis or pericarditis), GI (dysphagia)

**F. Polymyalgia Rheumatica:** stiffness and muscle pain in shoulders and hips, may be associated with temporal arteritis (high yield!)

**G. Ankylosing Spondylitis:** look for young male with bilateral sacroiliitis, "bamboo spine" on radiograph, HLA-B27 (+)

1. One of the seronegative spondyloarthropathies; others are reactive arthritis, psoriatic arthritis, IBD-associated arthritis

**H. Vasculitides**

1. Young adult with saddle nose deformity, sinusitis, hemoptysis, hematuria: Wegener granulomatosis (granulomatosis with polyangiitis)
2. Young male with arthritis, abdominal pain, hematuria, palpable purpura on lower extremities: Henoch-Schönlein purpura
3. Middle aged adult with granulomas, asthma, eosinophilia, neuropathy, and glomerulonephritis: Churg-Strauss
4. Patient with glomerulonephritis and lung involvement, pauci-immune inflammation on arteriole biopsy: microscopic polyangiitis

5. Elderly female with headaches, fatigue, jaw claudication: temporal arteritis (giant cell arteritis); will see very elevated ESR, start steroids *then* biopsy the temporal artery to confirm the diagnosis (if not treated immediately, feared complication is blindness); associated with polymyalgia rheumatica
6. Young Asian female with joint pain, unequal pulses in extremities: Takayasu arteritis
7. Middle aged male with HBV infection and renal failure, abdominal pain, testicular pain, no lung involvement: polyarteritis nodosa; renal angiogram will show microaneurysms and focal narrowing of vessels
8. Young smoker with gangrene of digits: Buerger disease (thromboangiitis obliterans), treatment is smoking cessation

### III. Important antibodies to recognize (Table 13-15)

## Ambulatory Medicine

*Some students wish they had briefly reviewed some ambulatory medicine prior to taking the shelf examination. A quick review of screening guidelines as well as common outpatient presentations may be helpful for the examination, especially if you have not had an outpatient rotation yet.*

### I. Screening: follow the USPSTF recommendations, knowing that the shelf will not be 100% up to date

#### A. Cancer

1. Colorectal cancer (CRC): from age 50 to 75, colonoscopy every 10 years, sigmoidoscopy every 5 years with fecal occult blood test (FOBT) every 3 years, or FOBT every 1 year
  - a. First-degree relative with CRC or adenomatous polyps (one relative <60, or two relatives any age), colonoscopy at age 40 (or 10 years before youngest diagnosis in family) then every 5 years
  - b. Family history of FAP, genetic testing at age 10, consider colectomy, colonoscopy every 1 to 2 years at puberty
  - c. Family history of HNPCC: genetic testing at age 21, colonoscopy every 2 years till 40 then every 1 year
  - d. Ulcerative colitis: colonoscopy 8 years after diagnosis, then every 1 to 2 years
  - e. If personal history of CRC or polyps, then more frequent screening
2. **Cervical Cancer:** from age 21 to 29, Pap smear every 3 years; age 30 to 65, Pap smear every 3 years or Pap + HPV genotyping every 5 years; age >65, stop testing if last three tests negative (or last two tests negative within past 10 years)
3. Breast cancer: from age 50 to 74, mammogram every 2 years (however, Department of Health and Human Services uses 2002 recommendation in adopting the ACA for screening at age 40 every 1 to 2 years)



**Table 13-15 Antibodies and Their Associated Conditions**

| <b>Antibody</b>                                                       | <b>Associated Conditions</b>                  |
|-----------------------------------------------------------------------|-----------------------------------------------|
| ANA                                                                   | SLE (many others)                             |
| Anti-Sm, anti-dsDNA                                                   | SLE                                           |
| Anti-histone                                                          | Drug-induced SLE                              |
| Anti-cardiolipin, lupus anticoagulant, anti- $\beta$ 2 glycoprotein-I | SLE, antiphospholipid syndrome                |
| RF                                                                    | RA (Sjögren syndrome, many others)            |
| Anti-CCP                                                              | RA                                            |
| Anti-SSA/SSB (anti-Ro/anti-La)                                        | Sjögren syndrome (SLE)                        |
| Anti-Scl70                                                            | Diffuse systemic sclerosis                    |
| Anti-centromere                                                       | Limited systemic sclerosis (CREST)            |
| Anti-Jo                                                               | Polymyositis/dermatomyositis                  |
| c-ANCA (anti-PR3)                                                     | Wegener granulomatosis                        |
| p-ANCA (anti-MPO)                                                     | Microscopic polyangiitis, Churg–Strauss       |
| Anti-RNP                                                              | Mixed connective tissue disease (SLE, others) |
| Anti-GBM                                                              | Goodpasture syndrome                          |
| Anti-desmoglein                                                       | Pemphigus                                     |
| Anti-mitochondrial                                                    | Primary biliary cirrhosis                     |
| Anti-gliadin, anti-endomysial, anti-transglutaminase                  | Celiac disease                                |
| Anti-TSH receptor                                                     | Grave disease                                 |
| Anti-TPO, anti-thyroglobulin, anti-microsomal                         | Hashimoto thyroiditis                         |

4. Prostate cancer, pancreatic cancer: insufficient evidence; USPSTF now recommends against prostate cancer screening using PSA (2012, grade D recommendation)
  5. Lung cancer: for the shelf, correct answer will be no evidence for screening; however, the USPSTF recently issued recommendations for annual low dose CT for age 55 to 80 with 30 pack-year history who currently smoke or quit within past 15 years (the shelf always lags behind current guidelines by a few years)
- B. STIs**
1. HIV: from age 15 to 65, all patients; screen anyone at increased risk (no matter the age)
  2. *Chlamydia* and gonorrhea: age 24 and younger, all sexually active women; all women aged >24 with risk factors
    - a. insufficient evidence to recommend this screening for men
  3. Asymptomatic men and women with risk factors should be screened for syphilis
- C. Abdominal Aortic Aneurysm:** from age 65 to 75, in men who have ever smoked, one time abdominal ultrasound
- D. Dyslipidemia:** from age 35+, check lipids in all men every 5 years; from age 45+, all women at increased risk for CAD every 5 years
1. Screen earlier and more frequently in patients at risk for CAD
- E. Osteoporosis:** from age 65+, DEXA scan for all women
- F. HTN:** from age 18+, screen for high blood pressure
- G. Diabetes Mellitus**
1. Screening: ADA recommends screening all adults with BMI  $\geq 25 \text{ kg/m}^2$  + 1 risk factor every 3 years with a hemoglobin A1c, fasting plasma glucose, or a 2-hour oral glucose tolerance test
  2. Diabetic patients: yearly ophthalmology and podiatry referrals; keep LDL <100 and BP < 130/80 (changing per ADA, but remember shelf questions lag behind), screen for microalbuminuria (30 to 300 mg in 24 hours)
- H. Hepatitis B Virus:** screen all patients at risk (IV drug users, MSM, etc.)
- I. Hepatitis C Virus:** screen all patients born between 1945 and 1965 and those at risk
- J.** Routine screening for thyroid disease is not recommended

## II. Adult Vaccinations

- A. Flu:** annually
- B. Tetanus:** One-time substitution of Tdap for Td booster, then Td booster every 10 years
- C. Zoster:** one dose at age 60+
- D. Pneumococcal:** one dose PPSV (23-valent pneumovax) at age 65+, earlier for immunocompromised patients
- E. Varicella:** 2 doses for all adults without evidence of immunity
- F. HPV:** 3 doses for men and women aged 9 to 26
- G.** Consider childhood vaccines if patient has not received them (e.g., hep B)

## III. Common Outpatient Complaints and Differential Diagnosis

- A. Chronic Cough:** Three most common causes are postnasal drip, asthma, and GERD

**B. Headache**

1. Patient with sudden onset worst headache of their life: subarachnoid hemorrhage; give calcium channel blocker to prevent cerebral vasospasm
2. Patient with unilateral headache preceded by seeing spots, occurs with photophobia: migraine
3. Patient with headache described as stabbing retro-orbital pain that has occurred every night for the past week: cluster headache
4. Patient with bilateral “pressure-like” headache occurring after long day of work: tension headache

**C. Dyspepsia:** epigastric pain, discomfort, bloating, “indigestion,” etc., with many etiologies

1. Functional dyspepsia: no associated ulcers, may be caused by gastric dysmotility or afferent nerve hypersensitivity
2. GERD
3. PUD
4. Other important causes: gastric cancer, medications, diabetic gastroparesis

**D. Hypertension:** most cases are primary (essential hypertension); important secondary causes include renal artery stenosis, OSA, renal failure, polycystic kidney disease, pheochromocytoma, Cushing syndrome, hyperaldosteronism, acromegaly, coarctation of the aorta, and medications

1. Complications: cardiac disease, renal failure, stroke, retinal disease
2. Antihypertensive medications and adverse reactions
  - a. Diuretics
    - Loop diuretics (furosemide): hypokalemia, acute interstitial nephritis, ototoxicity, gout, hypocalcemia (increased calcium excretion)
    - Thiazide diuretics: hypokalemia, hyperglycemia, hyperlipidemia, gout, hypercalcemia (increased calcium reabsorption)
  - b. ACE inhibitors: great choice in diabetics (reduce risk of diabetic nephropathy); adverse effects include hyperkalemia, cough, angioedema (c1 esterase inhibitor deficiency), acute renal failure (bilateral renal artery stenosis)
  - c.  $\beta$ -blockers: bradycardia, bronchospasm (if agent blocks  $\beta_2$  receptors), fatigue, depression, mask hypoglycemic symptoms if diabetic
  - d. Calcium channel blockers: peripheral edema

**E. Low Back Pain:** red flags to look out for include cauda equina syndrome (lower extremity weakness/numbness, incontinence, saddle anesthesia), cancer (history of cancer, weight loss, persistent pain, night or rest pain), infection (fever, IV drug user, recent surgery or bacterial infection, immunocompromised), fracture (osteoporosis, use of steroids, trauma), AAA (pulsating abdominal mass, history of atherosclerosis)



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